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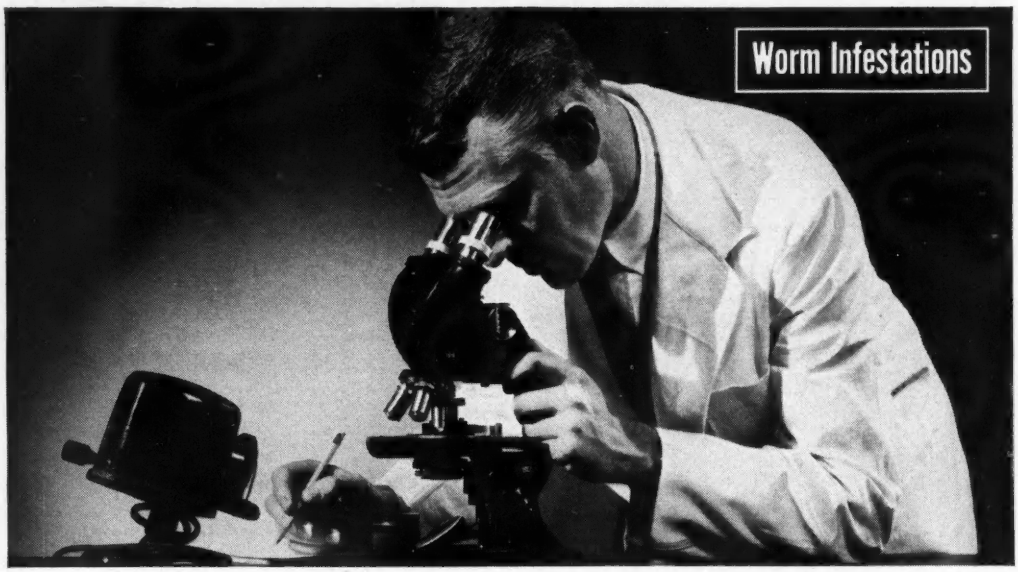

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Experiences with Cortisone Given Orally

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SUMMARY

The advantages of the oral administration of cortisone, when compared with cortisone given intramuscularly, include the more rapid appearance of therapeutic effects, which is of importance in the therapy of acute disease, and the faster dissipation of effects when the hormone is discontinued, which is of value when dangerous reactions occur. Oral dose schedules depend upon the degree of urgency or chronicity of the treated disease. In acute diseases the therapeutic results, in general, were disappointing. Cortisone may be of greater value in the long-term maintenance treatment of certain chronic diseases. By long-term therapy the authors mean practically continuous treatment until either the disease goes into spontaneous remission or undesirable effects of the drug require cessation of treatment. Critical selection of patients and constant supervision of therapy are vital to the successful administration of cortisone. Even with these precautions, however, the therapeutic use of cortisone must be regarded as experimental until the passage of time permits better appraisal of harmful effects.

APPROXIMATELY one year ago, the efficacy of orally administered cortisone was first reported.[4, 10] The numerous accounts of its spectacular therapeutic effects have popularized the use of cortisone to such an extent that in many instances it is wasted on patients indiscriminately selected for treatment. The fact that it may be administered conveniently and effectively in oral doses has often encouraged the improper use of the drug.

A detailed discussion of the effects of cortisone in specific diseases is not intended in this report; instead, emphasis will be put upon certain basic principles concerning the administration of cortisone by the oral route.

COMPARISON OF ORAL AND INTRAMUSCULAR ROUTES

In the administration of cortisone, the oral route has certain advantages over the intramuscular route which make the use of the latter undesirable unless there are contraindications to oral therapy. It has been shown previously[2] that cortisone given in an effective dose by mouth produces therapeutic effects more rapidly (usually within 12 hours) than cortisone injected intramuscularly. Whether the tablets* or the injectable suspension in syrup is used, effec-

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Presented as part of a symposium on Cortisone and ACTH before the Sections on General Medicine and General Practice at the 80th Annual Session of the California Medical Association, May 13-16, 1951, Los Angeles.

* Cortisone tablets were made available through the courtesy of Dr. A. Gibson, executive director, Medical Division, Merck & Company, Inc.

tive oral doses have been no more than 30 per cent greater than those given parenterally.[2]

The promptness of the therapeutic effect of cortisone given orally indicates that this hormone is absorbed more rapidly from the gastrointestinal tract than from intramuscular depots. This is obviously an important advantage in the treatment of acute diseases.

A second advantage of the oral over the intramuscular route is the brief duration of action.[2] For example, when therapy with oral doses of cortisone is discontinued, or if the dose is reduced to suboptimal levels, relapse usually occurs within 24 hours. In contrast, experience has shown that when cortisone has been injected intramuscularly, the effects often persist for several days following cessation of the drug. The brevity of action of the oral dose is of value, since it permits prompt termination of the effects of cortisone should signs of danger develop. Because of the rapid dissipation of an oral dose, cortisone administered by this route is given three or four times daily to maintain a constant therapeutic effect.

The clinical impressions of the speed of absorption and excretion of orally administered cortisone have been substantiated by recovery experiments.[13] Time of appearance and rate of excretion of cortisone in the urine following oral administration have been measured. It has been shown that cortisone appears in the urine within ten minutes of its ingestion, while no measurable cortisone appeared at any time during the intramuscular administration of 200 mg. of cortisone in 24 hours. It is assumed that the rate of absorption of cortisone from intramuscular depots is so slow that the amount of the drug in the blood never reaches a level (renal threshold) at which it is excreted through the kidneys. Cortisone disappears from the urine within 48 hours after termination of administration by the oral route.

CONTRAINDICATIONS TO CORTISONE THERAPY AND SELECTION OF PATIENTS

In the selection of patients for therapy with cortisone certain contraindications must be considered. Any significant degree of emotional disturbance renders the use of cortisone undesirable.[15] Many of the serious psychiatric complications in patients treated with cortisone have been observed in persons who were unstable prior to treatment. Because of the effect of cortisone on electrolyte and water metabolism,[18] patients with renal insufficiency and diminished cardiac reserve should not be given the hormone. The effect of cortisone upon blood pressure[18] makes hypertensive persons poor candidates for treatment. Although diabetes mellitus can be controlled with adjustment of insulin dosage,[1] the aggravation of this disease by cortisone makes its use inadvisable in diabetic patients. Cortisone is also contraindicated in patients with a history of peptic ulcer because of the reported deleterious results.[14] The hormone has been shown to intensify experimentally induced tuberculosis in animals;[7] consequently, it should not be given clinically to patients with active or latent tuberculosis until more is known of its effects. Cortisone inhibits growth in young animals[19] and therefore must be used cautiously in children when long-term therapy is contemplated.

The following clinical observations were made during the past year on 77 patients selected from the Veterans Administration Hospital, San Francisco, and from private practice for treatment with cortisone. The patients were divided into two groups. The first group consisted of 28 patients with acute diseases, selected for short-term treatment. The second group contained 49 patients with chronic diseases for which long-term treatment was contemplated. No patient with any of the stated contraindications was included in this study. Each patient with chronic disease was first given conservative conventional treatment and was treated with cortisone only after the therapeutic response to the older methods had been unsatisfactory.

DOSE, ADMINISTRATION, AND THERAPEUTIC RESULTS

In the treatment of acute diseases, in order to obtain rapid and maximal therapeutic effect, large initial oral doses of cortisone were used—approximately 300 mg. daily—with a gradual reduction in amount as symptoms regressed. In the present series, the total dose for patients with acute diseases varied between 700 and 4,600 mg. over a period of five to 23 days (see Table 1). In acute gouty arthritis, acute bursitis, status asthmaticus, dermatitis venenata, exfoliative psoriasis, and acute eczematoid dermatitis the therapeutic results, in general, were disappointing. Although subjective, and even objective, improvement occurred in most patients, recovery was seldom accelerated and complete recovery was infrequent.

In the long-term treatment of chronic diseases, it was found unnecessary to use large "priming doses" of cortisone. A daily dose of 100 mg. was satisfactory in most cases. In the group of patients with

TABLE 1.—*Therapeutic Results of Oral Cortisone in Certain Acute Diseases*

Diagnosis	Total No. of Patients	Excellent Results*			
		No. of Patients	Per Cent of Total	Total Dose, mg.	Days of Treatment
Acute gouty arthritis	11	5†	45%	1,045-2,585	8-22
Acute bursitis, shoulder	8	4	50%	984-1,500	5-12
Acute bursitis, trochanteric	1	0	0	1,075	10
Status asthmaticus	3	0	0	700-1,750	7-12
Dermatitis venenata, severe	2	0	0	1,300-1,575	9-12
Exfoliative psoriasis	2	0	0	4,200-4,600	21-23
Acute eczematoid dermatitis	1	0	0	1,950	10

* Prompt recovery without relapse after withdrawal of cortisone.

† Each patient received colchicine, 1.5 mg. daily, beginning on the third day of cortisone therapy.

chronic diseases, the initial daily dose was slowly reduced after the first two or three weeks of treatment in order to establish the minimal amount for effective maintenance. In most instances, it was found to range from 50 to 75 mg. daily.

In such long-term therapy, no effort was made to keep the patient symptom-free. "Maintenance dose" as the term is here used is that amount of cortisone which produces the desired therapeutic functional result, but which, at the same time, permits a minimal break-through of the symptoms and signs of disease. It is believed that this procedure provides not only for greatest economy in the use of the drug but also for reduction in the incidence of harmful effects. It must be emphasized that the size of the maintenance dose is not necessarily static and is always subject to change; it should fluctuate according to the spontaneous improvement or relapse which characterizes most chronic diseases.

Continuous long-term maintenance therapy for as long as 21 months was successfully maintained in 49 patients with rheumatoid arthritis, chronic gouty arthritis, bronchial asthma, atopic keratitis, chronic urticaria, chronic eczematoid dermatitis, sarcoidosis, Addison's disease, and sympathetic ophthalmia (Table 2). Ten of these patients had received intramuscular injections of cortisone prior to the introduction of oral therapy. No claim is made for the superiority of orally administered cortisone over well-established therapeutic regimens in the treatment of these diseases; it is simply pointed out that cortisone administered over a period of three months or longer successfully controlled the disease in a substantial number of patients.

PRECAUTIONS AND UNDESIRABLE EFFECTS

Routine hospitalization should not be required for the institution of therapy with cortisone. However, most of the patients in the present series were hospitalized during the first two weeks of treatment, and they were observed subsequently on an outpatient basis. In most of a previously reported series of cases,[3] a variety of laboratory tests were done both before and during administration of the hormone, but little positive information was thus obtained. As a result, the studies done before cortisone was used were later limited to routine weight and blood pressure readings, an x-ray film of the chest, an electrocardiogram, a serum cholesterol determination and a single postprandial blood glucose determination. A low salt diet was not prescribed routinely except when cortisone was given in large doses. At that time, in addition to salt restriction, potassium salts were given prophylactically.

Observations during the administration of cortisone were important and simple. The patient was questioned for unusual mood-swings. Overstimulation and depression frequently revealed early evidence of psychic disturbance. Often, rounding of the face, changes in body contour, and other evidence of hyperadrenalism were noted. Repeated determination of blood pressure disclosed diastolic hypertension in many instances. Downward revision of the dose of cortisone caused most of these undesirable effects to disappear, except the moon face. Sudden increase in weight, requiring restriction of salt and use of a mercurial diuretic, rarely occurred in patients receiving low maintenance doses of cortisone.

Determinations for sugar in the urine were done bi-weekly on all patients. In two patients with glycosuria, normal blood glucose levels revealed a lowered renal glucose threshold. Increasing blood cholesterol levels up to 436 mg. per 100 cc. were noted in four of 20 patients so tested. The significance of this increase is unknown. Hyperglycemia and hypokaliemia did not occur. Other possible complications of therapy with cortisone, such as psychoses,[15] convulsive seizures,[17] congestive failure,[8] vascular thromboses,[3] masked infection,[3] and interference with healing,[3] were not observed. Cushing's facies was commonly present, but it was not regarded as an indication for termination of cortisone. In only three cases was it considered necessary to discontinue the hormone because of untoward effects which persisted despite downward adjustment of dose. These effects included hypertension in one case, mild depression in another, and severe anxiety in the third. In these three cases the duration of treatment was five months, 12 months, and 10 days respectively. All the undesirable effects of cortisone disappeared when administration of the hormone was discontinued.

It seems likely that the infrequency of severe undesirable effects was due, at least in part, to careful selection of patients, to the coincidental exclusion of patients with diffuse vascular disease,[16] and to the use of small maintenance doses of cortisone. The simple precautions taken during the administration of cortisone also played an important part in the control of serious side effects. When treatment with cortisone was started, the patient was examined at

TABLE 2.—*Examples of Continuous Oral Cortisone Therapy for Three Months or Longer with Satisfactory Maintenance of Improvement*

Diagnosis	Number of Patients	Months* of Treatment	Daily Maintenance Dose, mg.
Rheumatoid arthritis	12	3-6	25-87.5
Rheumatoid arthritis	15	6-12	12.5-87.5
Rheumatoid arthritis	8	12-21	32-100
Chronic gouty arthritis	2†	9-13	37.5-75
Bronchial asthma	2	8-12	37.5-75
Atopic keratitis and dermatitis	1	7	125
Chronic urticaria, cause unknown	1	4	40
Chronic eczematoid dermatitis	2	7	75
Sarcoidosis	2	3-4	40
Addison's disease	2	6-10	25
Sympathetic ophthalmia	2	4-5	25-100

* Patients receiving cortisone for more than 11 months were previously given cortisone intramuscularly.

† Each patient received colchicine, 1 to 1.5 mg. daily.

TABLE 3.—*Eosinophil Response to Daily Slow Intravenous ACTH, 25 mg., in Rheumatoid Arthritis Patients Receiving Continuous Cortisone Therapy for 4 to 7 Months*

Patient	Daily Dose of Cortisone (mg.)	Months of Cortisone Therapy	Intravenous ACTH: Duration of Daily Intravenous Injection (Hours)	Intravenous ACTH: Day of Eosinopenic Effect	Intravenous ACTH: Eosinophil Counts on Day of Significant Decrease: Pre-ACTH	Post-ACTH	Per Cent Decrease
I. B.	56	4	12	1st	99	11	89
N. H.	64	7	12*	2nd	198	16	92
G. J.	50	5	12	1st	330	88	74
F. K.	75	7	6	1st	209	84	60
B. L.	66	6	12	2nd	132	11	92
I. L.	50	4	6	2nd	150	41	73
M. M.	62½	7	12*	2nd	431	31	93

* Duration of intravenous injection ACTH on previous day had been 3 hours.

TABLE 4.—*Eosinophil Response to Daily Slow Intravenous ACTH, 25 mg., in Rheumatoid Arthritis Patients Receiving Continuous Cortisone Therapy for 9 to 14 Months*

Patient	Daily Dose of Cortisone (mg.)	Months of Cortisone Therapy	Intravenous ACTH: Duration of Daily Intravenous Injection (Hours)	Intravenous ACTH: Day of Eosinopenic Effect	Intravenous ACTH: Eosinophil Counts on Day of Significant Decrease: Pre-ACTH	Post-ACTH	Per Cent Decrease
E. B.	50	11	12	2nd	374	110	71
F. H.	37½	14	3	2nd	330	88	74
A. L.	75	14	12	2nd	220	70	69
L. L.	87½	10	3	2nd	220	82	63
W. L.	100	14	12*	4th	209	60	72
E. M.	75	11	12*	2nd	431	31	93
J. R.†	37½	9	12	2nd	572	27	95

* Duration of intravenous injection ACTH on previous day(s) had been 3 hours.
† Diagnosis: chronic bronchial asthma.

least once daily. Patients receiving maintenance doses of cortisone were observed at least once weekly, not only for early signs of toxicity but also in order to reevaluate the maintenance dose requirements.

Adrenocortical atrophy has been described[11] following administration of large doses of cortisone and is presumably due to suppression of pituitary secretion of adrenocorticotropic hormone. This factor has led to the recommendation of periodic withdrawal of cortisone or alternating courses of cortisone and ACTH.[9] In this study, however, cortisone was deliberately administered continuously—without alternate courses of ACTH—to patients requiring maintenance therapy. Except for occasional mild weakness, no clinical evidence of adrenocortical insufficiency was encountered.

Gordon[6] and co-workers recently reported that the continuous, slow intravenous administration of ACTH stimulates the adrenal cortex much more effectively than ACTH given intramuscularly. Maximal adrenal stimulation by any given dose of ACTH is obtained when the hormone is given by the constant drip technique over a period of 12 to 24 hours. The effectiveness of this method of adrenal stimulation decreases as the duration of the intravenous injection decreases. Nevertheless, in patients with normal adrenal function, Krupp and Engleman[12] observed a consistent, excellent response to 25 mg. of ACTH when it was given intravenously over a period of three hours.

In order to evaluate their adrenocortical function, 14 of the patients given cortisone for long terms were given ACTH intravenously for periods varying between three and 12 hours. In each patient so tested, adrenocortical function was manifested by excellent eosinopenic response to ACTH, despite the continued ingestion of cortisone (Tables 3 and 4). It appears that irreversible adrenal atrophy is not a likely result of long-term treatment with cortisone when the prescribed maintenance doses are used. It must be noted, however, that more than one intravenous injection of ACTH was often required in order to demonstrate adrenal responsiveness. The slower than normal response to intravenous ACTH is compatible with the observation[18] that there is a depression of adrenal cortex function during therapy with cortisone even when small doses of cortisone are used. It therefore follows that it is necessary to be constantly alert during cortisone therapy for periods of severe stress and the patient's possible need of more cortisone, or even ACTH. Furthermore, sudden withdrawal of cortisone should be avoided. Gradual reduction of the daily oral dose of cortisone prior to the termination of treatment may permit the secretion of endogenous ACTH and the return of normal adrenal function, so that symptoms of adrenocortical insufficiency will not appear. Failure to do so in a patient recently called to the authors' attention[5] resulted in an Addisonian crisis. It has been the authors' practice to reduce the daily dose by 12.5 to 25.0 mg. every two or three days

before complete withdrawal of the hormone. The concomitant use of ACTH may also be of value during cortisone withdrawal.

DISCUSSION

Cortisone administered by the oral route appears to be an invaluable addition to the therapeutic armamentarium. The hormone may be of particular value in the long-term maintenance treatment of chronic diseases. By long-term therapy, we mean practically continuous treatment until either the disease goes into spontaneous remission or undesirable effects of the drug require cessation of treatment. This implies that the patient can financially afford such long-term therapy and that the future supply of the hormone is assured; otherwise, treatment of chronic diseases with cortisone should not be considered. It is emphasized that critical selection of patients and constant supervision of therapy are vital to the successful administration of cortisone. Even with these precautions, however, the therapeutic use of cortisone must be regarded as experimental until the passage of time permits better appraisal of harmful effects. It is the authors' opinion that, with the exception of the critically ill patient in such precarious condition that heroic treatment is required, all patients should be given a reasonable period of conventional therapy before treatment with cortisone is instituted. If the disease progresses despite these measures, and assuming that the patient has a disease known to respond favorably to the hormone, the therapeutic use of cortisone may then be considered.

655 Sutter Street.

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Experience with Cortisone and ACTH in a Private Clinic

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SUMMARY

Cortisone and ACTH are valuable agents for treating a large variety of diseases. In appropriate situations they may save life. It may be possible to prevent loss of vision in eye disease or permanent damage to important viscera in generalized disease. With ready access to these agents through the pharmacist, it is important to know that cortisone and ACTH can be used in office practice provided patients are selected carefully and followed frequently and closely. Strict observation of criteria for selection of patients limited the size of the series of patients reported upon, but by the same token the incidence of complications from therapy was exceptionally small. Every physician who elects to employ these potent hormones must become familiar with their physiological effects and with the various methods of exhibiting them. Some of these effects are noted in this paper, but the experiences reviewed here provide an incomplete picture of the wide application of cortisone and ACTH.

EVERYONE is familiar with the discovery of the therapeutic effects of adrenocorticotropic hormone (ACTH) and of cortisone by Hench and coworkers.[3] Two years of clinical application of these hormones can be summarized in a general way:

1. These agents can provide palliation of uncomfortable and damaging effects of many non-endocrine diseases. The basis for the action of these drugs in such diseases appears to be pharmacodynamic rather than humoral.

2. In a disease of brief duration, such as certain drug sensitivity reactions or an isolated attack of uveitis or of rheumatic fever, the clinical manifestations can often be subdued until the process has run its course and therapy can be stopped safely..

3. Undesirable physiologic effects of large doses of adrenal steroids often appear, and, therefore, the problem of prolonged therapy may become extremely complicated. In many instances, however, doses of either hormone sufficient to provide a desirable therapeutic effect produce no undesirable effects, and prolonged therapy is possible.

4. Upon withdrawal of the drugs, clinical manifestations of chronic active disease return, usually with intensity comparable to that preceding therapy. Fortunately, undesirable "toxic" responses regress or disappear upon cessation of therapy.

5. Specific contraindications to use of these agents have been delineated.

For a little more than a year both ACTH and cortisone have been used by the authors in treating a series of carefully selected patients with a variety of diseases (Table 1).

Patients with acute, serious illness of brief duration were treated after only preliminary investigation for possible contraindications to therapy. Patients with chronic disease or diseases for which therapy was to be on a trial basis were carefully screened for presence of renal or cardiac insufficiency, hypertension, diabetes, mental disease, active tuberculosis, and history of peptic ulcer. The occurrence of any of these during therapy was watched for with great care in the clinic and in the laboratory. To prevent undesirable retention of large amounts of sodium and water, diets containing 2

TABLE 1.—*Data on Patients Treated with Cortisone and with ACTH in the Period April 1950 to April 1951*

Disease	Result: Success	Result: Failure	Treated at: Hospital	Treated at: Office, Home
TREATED WITH CORTISONE				
Rheumatoid arthritis	11	0	2	9
Rheumatic fever	1	0	1	0
Acute bursitis	3	0	0	3
Calcific bursitis, chronic	0	1	0	1
Gout, acute	1	0	0	1
Chronic	1	0	0	1
Asthma	4	4*	4	8
Atopic dermatitis	3	0	0	3
Drug sensitivity reactions	5	0	5	0
Eye disease:				
Uveitis (including post-traumatic)	13	2	2	13
Keratitis	4	2	0	6
Optic neuritis (all types)	3	3	5	5
Thyroiditis, acute	1	0	0	1
Pulmonary beryllosis	1	0	0	1
TREATED WITH ACTH				
Intramuscular administration:				
Asthma, acute status	2	0	2	0
†Collagen disease	1	0	1	0
Chronic ulcerative colitis	1	0	1	0
Pulmonary beryllosis	1	0	0	1
Gout	1	1	0	2
Pericarditis, tuberculous	0	1	1	0
Psoriasis with arthritis	1	0	0	1
Intravenous administration:				
Asthma, acute status	3	0	2	2
Discoid lupus erythematosus	1	0	0	1
Chronic hepatitis in acute exacerbation	1	0	1	0
†Collagen disease	1	0	1	0

* Improved initially, but had relapse while on treatment.
† Same patient.

Presented as part of a symposium on Cortisone and ACTH before the Sections on General Medicine and General Practice at the 80th Annual Meeting of the California Medical Association, May 13-16, 1951, Los Angeles.

gm. or less of sodium chloride were prescribed. Potassium citrate in doses of 3 to 9 gm. (25 to 75 mEq.) a day was given to maintain potassium balance and to prevent, if possible, unusual nitrogen loss. Eosinophil counts were done periodically during the use of both hormones; although found useful in judging therapy with ACTH, they were abandoned in cortisone-treated patients.

TREATMENT WITH CORTISONE

During the first three months cortisone was used in the work here reported, it was given intramuscularly, usually in doses of 200 to 300 mg. the first day or two, and 100 mg. daily thereafter. From July 1950, the suspension was given orally to all patients who could accept oral therapy, first in syrup and later, when available, in tablet form. The daily oral dose was divided into four or three doses given at five-hour to eight-hour intervals during the waking hours. Oral doses of cortisone usually totalled 200 mg. the first day, followed by 100 mg. daily thereafter until the desired clinical effect was assured. The daily dose was then reduced by 12.5 mg., maintained at the new level for several days, then reduced another 12.5 mg. and so on until the minimal effective dose was ascertained. Rarely a patient would require more than 100 mg. daily to produce a therapeutic effect. In no instance was it necessary to use more than 150 mg. daily, although it is recognized that larger doses may be required for some patients. Doses of 75 to 100 mg. were usually necessary to control clinical manifestations of disease; only one patient with chronic gout required less. Withdrawal of cortisone after three to four weeks of therapy was accomplished by diminishing the dose by 25 mg. every three to four days. With this schedule of therapy no signs of post-cortisone adrenocortical hypofunction were noted.

Rheumatoid Arthritis: The experience with cortisone in this disease was similar to that recorded elsewhere. Eleven patients were treated with doses of 75 to 100 mg. daily for over four months with no evidence of "toxicity" or of development of adrenal atrophy. Two patients did not benefit sufficiently to warrant continuous therapy. In one case mild hypertension developed, and when edema also developed despite careful salt restriction, use of the drug was discontinued.

Rheumatic Fever: One patient, a girl aged 11 with acute rheumatic fever and carditis, was treated with cortisone. Within the first 24 hours, while receiving 200 mg. of cortisone orally, she became afebrile, an aortic diastolic murmur disappeared, and the electrocardiogram returned to normal. An apical diastolic murmur was unchanged. The patient received 100 mg. daily for four days, then 87.5 mg. for four days and finally 75 mg. daily for a total of 28 days followed by gradual reduction of dose without recurrence of acute disease. It is too early to assess the effect of the drug on development of valvular disease. For this patient rheumatic fever was, for the most part, an asymptomatic rest in bed.

Acute Bursitis: On the suggestion of Engleman,[1] cortisone was used to treat one case each of acute subdeltoid bursitis, tennis elbow and subgluteal bursitis. A total dose of 1 gm. (200 mg. the first day, followed by 100 mg. a day for eight days) provided early remission of pain and return of motion in three patients. In a fourth patient with chronic calcific subdeltoid bursitis, treatment was unsuccessful.

Gout: One patient, aged 64, with chronic tophaceous gout of many years' duration was treated with cortisone, 50 mg. daily for 42 days, with complete relief. At last report he had been without therapy of any kind for eight weeks and remained well. Deformity from tophi and damaged joints was not altered, but the patient recovered from a totally disabled state to the point where he could attend his office and play golf. A second patient was treated for an acute, severe attack of gout that was unaltered by colchicine. He was given 200 mg. daily the first three days, followed by 150 mg. daily for five days with complete recovery. Colchicine, 0.6 mg. four times daily, was added after relief from cortisone had been obtained. A recurrence a month later was treated with ACTH.

Asthma: Eight patients with severe, chronic asthma were treated either for acute, threatening attacks of asthma or for chronic respiratory embarrassment that would not yield to proper conventional treatment even in the hospital. Four had fair response to cortisone in doses of 100 to 150 mg. per day, but received no benefit from smaller doses; treatment was abandoned in these patients. The other four responded remarkably well and have received intermittent therapy since then. One of them has had remissions of four to six weeks after each course of treatment, in contrast to a previous state of continuous asthma. Cortisone certainly is of value in the treatment of asthma, but failures are common and the problems of continuous therapy always present.

Atopic Dermatitis: Three patients with atopic dermatitis were treated for periods of two to six weeks with rapid and complete clearing of skin lesions. All had relapse within a few weeks after therapy was stopped, but in each case the relapse was not so severe as the previous disease.

Drug Sensitization: Four patients with serious sensitivity reactions to penicillin and one with a reaction to streptomycin received cortisone orally. All responded rapidly to an initial dose of 200 mg. the first day followed by 100 mg. daily for seven to ten days. Fever, exfoliation, erythema bullosum-like lesions, and edema cleared within 48 hours. The usually severe "toxic" course of such reactions can be reduced to a mild reaction that allows for rapid recovery once the offending agent has been removed or excreted.

Eye Disease: Twenty-seven patients were treated (Table 2). Fifteen of them had uveal tract disease (chorioiditis or iritis), and four of the patients in this group were treated only with eye drops of cortisone suspension in a concentration of either 2.5

per cent or 0.8 per cent. The drops were instilled hourly during waking hours for the first seven to 14 days, after which the interval was lengthened periodically until a maximum of four times a day was reached. At night an ophthalmic ointment (2.5 per cent cortisone) was used. Three of the four patients improved remarkably; one, only slightly. With cessation of therapy there was recurrence of clinical evidence of disease in three patients, but resumption of treatment controlled inflammatory signs until the disease had run its course and treatment could be stopped. In the ordinary case, three to six weeks of treatment was required. Local therapy alone may often induce rapid disappearance of keratitic precipitate, of vascular engorgement, of vitreous opacities and even of chorioidal lesions. Five patients not suited for oral treatment or local instillation of drops were given 0.5 cc. of the standard suspension of cortisone subconjunctivally every two to three weeks for three doses with rapid healing of acute, severe chorioiditis. Two patients with acute chorioiditis had prompt healing with use

TABLE 2.—*Treatment of Diseases of the Eye with Cortisone*

Diagnosis	Dose and Method of Administration	Response
Iridocyclitis, acute, bilateral	Intramuscular 2.1 gm. in 10 days	Rapid cure
Iridocyclitis, chronic, bilateral with rheumatoid arthritis	Oral 100 mg. daily continuously	Rapid improvement while on treatment
Chorioiditis, chronic, severe, 1 yr.	Intramuscular 100 mg. daily, 2 mo.; 300 mg. weekly 1 mo.	Marked improvement (cure?); all other treatment failed
Chorioiditis, chronic, severe	Intramuscular 100 mg. to 150 mg. daily	Exacerbation on 150 mg.; treatment stopped
Uveitis, chronic, with secondary glaucoma	Subconjunctival 0.5 cc. (12.5 mg.) every 3 wk. three times	Remarkable improvement; well with no treatment, 4 mo.
Chorioiditis, acute, severe	Subconjunctival 0.5 cc. (12.5 mg.) every 3 wk. three times	Remarkable improvement; healed 6 wk.
Iridocyclitis, post-traumatic	Subconjunctival 0.5 cc. twice	Cleared very rapidly
Iridocyclitis, post-traumatic	Subconjunctival 0.5 cc.	Rapid clearing of lesion
Vitreous hemorrhage, postoperative, 8 wk. duration	Subconjunctival 0.5 cc.; given deep, episcleral	Pronounced clearing in 5 days
Glaucoma, acute, secondary to iridocyclitis. (Due to histoplasmosis sensitivity?)	Eye drops (2.5%) every hr.; subconjunctival 0.5 cc.	Prompt and complete reversal of disease
Chorioiditis, acute, recurrent	Eye drops (2.5%) every hr.; subconjunctival 0.5 cc. every 2 wk. 4 times.	Slow, steady improvement; almost healed
Iridocyclitis, post-traumatic	Eye drops (2.5%) every hr.	Rapid recovery
Iridocyclitis, acute	Eye drops (0.8%) every hr.	Moderately good result
Iridocyclitis and keratitis, post herpes zoster	Eye drops (2.5%) every hr.	Good response with healing
Iridocyclitis, recurrent	Eye drops (0.8%) every hr.	Fair to no effect
Keratitis, severe (etiol?)	Eye drops (2.5%) every hr. for 3 wk.	Good response; little or no scar
Keratitis, bilateral, allergic	Eye drops (2.5%) every hr.; ointment (2.5%) at night	Excellent response
Keratitis, recurrent, (etiol?)	Eye drops (0.8%) every hr.	Rapid improvement
Keratitis, postoperative	Eye drops (2.5%) every hr.	Fair response, healing incomplete
Keratitis, dendritic, acute	Eye drops (2.5%) every 2 hr.; subconjunctival 0.5 cc. weekly	Symptomatic improvement; slow healing
Conjunctivitis, chronic; keratitis sicca, healed	Eye drops (0.8%)	Subjective improvement
Retrobulbar neuritis, acute	Intramuscular or oral 100 mg. daily for 20 days	Rapid improvement to 20/20 vision
Retrobulbar neuritis	Intramuscular 300 mg. daily for 2 days; 100 mg. daily for 14 days	Slow improvement to normal vision
Optic neuritis and neuroretinitis, bilateral, severe	Oral 100 mg. daily	Rapid improvement in 4 days; had not improved in 10 days prior to treatment
Retrobulbar neuritis	Oral 100 mg. daily for 14 days	Failure
Optic neuritis and papillitis, severe	Oral 100 mg. daily for 28 days; subconjunctival 12.5 mg.	Failure
Optic neuritis, acute; tenosynovitis, external rectus	Oral 100 mg. daily for 21 days; eye drops (2.5%) every hr.; ACTH 20 mg. intravenously daily for 3 days after cortisone treatment	Failure to all therapy; ACTH inadequate

of eye drops and subconjunctival injection. Of four patients treated with cortisone orally or intramuscularly in conventional manner, three had excellent response and one had recurrence of disease while still receiving the hormone.

Four patients with keratitis were treated successfully with cortisone eye drops; two others had little or no improvement on local or subconjunctival therapy.

Six patients received cortisone orally or intramuscularly for optic neuritis or retrobulbar neuritis. Only three improved while on cortisone; the other three were not helped.

Thyroiditis: A 52-year-old female with acute thyroiditis of two weeks' duration was given cortisone, 100 mg. daily for 10 days. After 36 hours of treatment the gland, which had been enlarged and very tender, was no longer painful and the temperature became normal. The thyroid gland diminished only slightly in size, but became firm. No complication such as dysthyroidism or dysphagia developed.

GENERAL OBSERVATIONS

Nineteen patients acutely ill with drug sensitivity reactions, severe rheumatoid arthritis, serious eye disease, and status asthmaticus were started on treatment in the hospital only because their condition was serious enough to justify hospitalization. Therapy was initiated in the office or home on an ambulatory basis in 27 patients treated with cortisone orally or parenterally, and in 17 patients with ophthalmic disease treated by local application of cortisone suspension. Patients were observed daily during the initial week of therapy and at less frequent intervals as treatment was prolonged. All patients were observed at least once a week for check on mental state, weight, blood pressure and glucose in the urine.

Treatment had to be stopped in only two cases because of undesirable reactions. In one case hyperglycemia with glycosuria and acetonuria developed. As cortisone had provided only minimal relief from asthma, cessation of therapy was acceptable to the patient. Acute rise of blood pressure to serious hypertensive levels prompted cessation of therapy in a patient with rheumatoid arthritis.

In one patient with rheumatoid arthritis and a decrease in glucose tolerance determined prior to treatment, mild hyperglycemia and persistent 1 to 2 plus glycosuria developed during maintenance on 100 mg. cortisone daily. At last report the patient had been under treatment for four months with satisfactory improvement in arthritis and no advance of the "steroid diabetes."

TREATMENT WITH ACTH

Because ACTH must be administered parenterally, only a few patients were treated with it prior to a few months ago. The basis for selection of patients was identical to that for cortisone therapy.

Diagnostic test for adrenal function: Eight patients were tested according to the method of Thorn, with a decrease in eosinophils in the blood the sole criterion. Often, the recommended dose of 25 mg. of ACTH intramuscularly did not produce a 50 per cent decrease in eosinophils in normal persons; a dose of 40 to 50 mg. was required.

Asthma: Two patients with status asthmaticus responded favorably within six to 12 hours to ACTH, 25 mg. intramuscularly every six hours. Therapy was stopped when the acute attack had completely subsided, usually in four to seven days.

Pericarditis: A 22-year-old student was treated for what was thought to be rheumatic fever with pericarditis. He received 25 mg. of ACTH intramuscularly every six hours. Fever disappeared, tachycardia diminished, but the pericardial rub persisted. Pericardiocentesis was done and sanguinous fluid was withdrawn. No organisms were grown on culture of the fluid. After five days fever returned and it was then concluded that the most likely etiologic factor was M. tuberculosis. ACTH was stopped and appropriate therapy instituted. There is no evidence that this brief exposure to ACTH was harmful; of interest was the rapid alleviation of pain, fever and tachycardia with persistence of the active disease.

Pulmonary Beryllosis: A 36-year-old neon sign worker with chronic pulmonary granulomatosis resulting from working with beryllium was treated with ACTH, 100 mg. intramuscularly daily, with rapid decrease in dyspnea, moderate increases in vital capacity from 2,800 cc. to 3,600 cc., and increased capacity for exercise. Appetite improved and there was a gain of 16 pounds in body weight. While the patient was being maintained on 30 to 40 mg. daily for eight weeks, there was gradual reversion to the pretreatment state of pulmonary insufficiency. An increase in dose was not thought to be safe in this patient. He did poorly when without treatment. Cortisone, 100 mg. daily, produced satisfactory improvement—almost comparable to the best state while on ACTH. The patient was maintained on cortisone for three months without incident. Use of the drug was then discontinued and at the time of last report the patient had been more comfortable for three months than at any previous time when not being treated. It is planned to continue with ACTH or cortisone in courses interspersed with rest periods.

Gout: Two patients had relief from acute attacks of gout following a single dose of 50 mg. of ACTH intramuscularly. Both were treated with colchicine, 0.5 mg. three times daily, in the hope that recurrence would be prevented. Another patient had no response to one dose of ACTH, 50 mg. intramuscularly. At the time of this report he was being studied further with larger doses.

Chronic Ulcerative Colitis: A 38-year-old female was treated with ACTH after four months of severe, acute exacerbation of chronic ulcerative colitis. The dosage was at the rate of 100 mg. daily for two and one-half days, then 80 mg. daily for two days, and

60 mg. daily for two days. Each day's dose was divided into four equal doses given six hours apart. The patient became afebrile in 24 hours. Vomiting ceased and diarrhea improved. After completion of this brief course of therapy the patient had only six or seven defecations a day instead of the 20 to 30 a day previously. After ten days of relative well-being, relapse occurred. It was recognized that so brief a course of ACTH therapy would not insure a lasting remission, but continued administration was impossible for financial reasons. The prompt response to ACTH in this case indicates that this agent offers advantage in the treatment of devastating exacerbations of ulcerative colitis and of regional enteritis.

INTRAVENOUS ADMINISTRATION OF ACTH

Following Gordon's report[2] at the second ACTH Conference, ACTH was given intravenously to a selected group of patients.* It has been confirmed that ACTH can be given safely intravenously. Great therapeutic effect results from doses of 10 to 25 mg. dissolved in 5 per cent glucose and given over a period of four to 16 hours. The longer the time of the infusion, the greater the physiologic response on the part of the adrenal cortex; the effect of a dose given intravenously may be equal to a daily intramuscular dose five to ten times greater.[2, 4] It is of great importance to prevent potassium depletion in patients given the substance intravenously. In the present series 25 to 50 mEq. of potassium (3 to 6 gm. potassium citrate) was given daily to all patients who received ACTH intravenously.

Test for adrenal insufficiency: A patient with asthma who had received cortisone, 100 mg. daily for six weeks, followed by two months of conservative therapy, had a severe, unremitting attack of asthma. In a routine Thorn test there was no decrease in eosinophils. A test with ACTH, 25 mg. given intravenously as a drip for four hours, produced a change in eosinophil count from 1,430 per cu. mm. to 123 per cu. mm. six hours after start of the infusion. The patient received the hormone intravenously daily for three days with complete relief from the attack.

Asthma: Three patients with severe, acute attacks of asthma were treated with 10 to 25 mg. of ACTH intravenously daily or every other day for three to six doses with excellent results. Two were treated in the hospital. One patient was treated in the office with 25 mg. in 500 cc. of 5 per cent dextrose in water given over a three- to four-hour period every other day.

Discoid lupus erythmatosus: A 27-year-old woman was treated with ACTH, 10 mg. every other day, given intravenously with infusion taking three to four hours. The patient became afebrile, and the generalized skin lesions rapidly regressed. Seven doses were given without appearance of undesirable effects. Relapse occurred after cessation of therapy, and the patient was given 10 mg. three times weekly for another four doses with excellent results. At last report, five weeks later, there was no relapse.

Chronic hepatitis in acute exacerbation: A 35-year-old woman who had an acute bout of virus hepatitis in October 1950, had a relapse late in November. She improved slowly and by February 1951 was considered to be almost well. In March she again became jaundiced, and because of fever, anorexia, intense jaundice and a greatly enlarged liver (the lower margin at the iliac crest) was placed in the hospital. Results of laboratory studies were indicative of seriously impaired liver function. The patient was not improved after ten days of rest and usual care. ACTH, 10 mg. daily in 1,000 cc. of 5 per cent dextrose in water, given intravenously over 12 hours, was begun on a trial basis. Within 48 hours the patient was afebrile and eating heartily. After five doses, the drug was withheld for one day, and the patient again was ill, febrile (102° F.) and could not eat. Next day, after receiving 5 mg. of ACTH intravenously in six hours she was again afebrile and had begun to eat. The improvement, clinically and by liver function appraisal, was remarkable while the daily infusions of 10 mg. ACTH were continued. After a total of 23 days of treatment, ACTH was stopped. At last report, three weeks later, improvement was continuing. It is likely that ACTH so suppressed the toxic, febrile manifestations of hepatitis that the patient was able to eat and to effect some sort of hepatic protective mechanism more readily.

Collagen disease: A 71-year-old male successfully treated with cortisone had relapse when cortisone was withdrawn. Four weeks later, in April 1951, exacerbation of rheumatoid disease occurred. With this there developed extensive involvement of synovia, pleura, pericardium, and skin, associated with fever and extreme debility. ACTH was given, 100 mg. daily intramuscularly, with rapid improvement. Reduction of the dose to 60 mg. daily was followed by exacerbation of disease. The patient was given ACTH, 25 mg. daily intravenously, with rapid improvement. At last report he had been maintained on ACTH intravenously daily for ten days — the dose then was 20 mg. daily—and was much improved objectively and subjectively.

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* This work was done in collaboration with E. P. Engleman, M.D.

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Experience with ACTH and Cortisone in Private Practice

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SUMMARY

ACTH and cortisone are highly nonspecific in their action. A fundamental portion of the mechanism of action is the interposition of a blockade between toxin and end organ. This effect can be of great benefit in the management of a variety of acute and chronic diseases.

A major hazard constantly to be kept in mind is the potential masking of advancing disease. This consideration makes concomitant chemotherapy mandatory in the presence of specific infections.

In chronic diseased states it should be assumed that prolonged therapy will be necessary. Treatment should not be instituted unless such continued therapy is physiologically and economically feasible.

THE clinical use of adrenocorticotropic hormone (ACTH) and cortisone is still in the experimental stage. Thus far there is no evidence to show that any disease is cured by use of the hormones. These agents have been shown to have widespread application in treatment of allergic diseases, in certain infectious diseases, and in the poorly defined syndromes classified as "collagen diseases." In all these diseases the common denominator appears to be the establishment of a blockade between toxin and end organ.

ACTH and cortisone have been found to be most useful in Addison's disease (cortisone only), functional adrenocortical insufficiency, functional hypopituitarism, anorexia nervosa, idiopathic hypoglycemia, acute rheumatic fever, acute gouty arthritis, status asthmaticus, serum sickness, exfoliative dermatitis, Loeffler's syndrome, acute inflammatory diseases of the eye, burns and frost bite, poison ivy dermatitis, and allergic diseases in general. The agents may be useful in rheumatoid arthritis, psoriasis, disseminated lupus erythematosus, dermatomyositis, periarteritis nodosa, acquired hemolytic jaundice, vasomotor rhinitis, urticaria, multiple myeloma, the lymphomata, nephrotic syndrome, ulcerative colitis, regional enteritis, pulmonary beryllosis and in controlling the symptoms of drug addiction. They are of questionable value in mental disease, multiple sclerosis, pemphigus, scleroderma, myasthenia gravis, osteoarthritis, Paget's disease, thyrotoxicosis, malignant exophthalmos, glomerulonephritis, cancer and (cortisone only) hypertension.

Their use is contraindicated in the presence of diabetes mellitus, Cushing's syndrome, hypertension (ACTH), congestive heart failure, osteoporosis, acne, hirsutism, pathological fluid collection, tuberculosis, fresh wounds and gastric or duodenal ulcer. In certain circumstances, however, indications for administration of these hormones may exist despite such contraindications.

The mode of action of these hormones remains obscure. In general the cortical hormones like other hormonal agents regulate specific enzymatic activity, which may proceed in their absence. The hormones may remove circulating toxins by adsorption, may produce a blockade at the level of the cell membrane, or may directly protect enzymatic systems within the cell itself. It is felt by some investigators that by interposing a blockade between toxin and specific end organ a respite is afforded the organism and that such a respite may permit specific immune reactions to effect a cure as in the case of infectious diseases, or may help to initiate a prolonged remission as in asthma and some forms of leukemia. In order to effect a significant remission in certain chronic conditions in which these agents are effective, prolonged administration has been found necessary in a high percentage of cases.

Data on certain important considerations regarding comparative effects of the two drugs on both the adrenal cortex and the pituitary gland, the rate of absorption, and the incidence of foreign protein reactions, are given in Table 1.

ACTH is effective only by intramuscular or intravenous administration. If the intramuscular route

TABLE 1.—*Comparison of Effects of ACTH and Cortisone*

	ACTH (30 to 50 mg.)	Cortisone (100 mg.)
Effect on adrenal cortex	Stimulation	Inhibition
Effect on pituitary gland	Inhibition	Inhibition of ACTH secretion
Routes of administration:		
a. Oral	Ineffective	Potent
b. Intramuscular	Rapid and of short duration, 2 to 4 hr.	Slow (1 or 2 doses daily)
c. Intravenous	Rapid and prolonged	Contraindicated
Development of sensitivity	Occasional	Rare

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is used the total daily dose should be divided equally and administered at six-hour intervals to obtain the maximal therapeutic effect.

For intravenous use the most effective procedure is by continuous slow drip through the 24 hours. It appears probable that in the immediate future the intravenous route will be used for maximal immediate effect, and long-acting oily suspensions will be used for long-term maintenance therapy.

Cortisone may be administered either parenterally or orally. When used intramuscularly, doses may be given once or twice daily. In oral administration the material may be given at six-hour intervals.

The average initial daily dose of ACTH should be 80 to 100 mg. and of cortisone 300 mg. The average maintenance dose of ACTH is 30 to 50 mg., and of cortisone 50 to 100 mg.

At times it may be advisable to combine or alternate the hormones. Intermittent administration of one or both may result in the development of resistance. A gradual decrease in dosage is preferable to intermittent administration in most instances. Simultaneous administration of both or alternating ACTH and cortisone therapy sometimes is more effective than giving one or the other alone. Rest periods are indicated when cortisone alone is used, because of possible adrenocortical atrophy. Such rest periods permit resumption of adrenocortical activity which may have become depressed during cortisone administration. These rest periods should not be less than four to six weeks. A full course of treatment should cover two to six weeks and the total dosage of cortisone should not exceed 3 to 4 gm. Simultaneous administration of desiccated thyroid may be necessary for some patients undergoing prolonged therapy, because of possible inhibition of thyroid-stimulating hormone.

COMPLICATIONS

Hypertension, hyperglycemia, fluid retention and psychosis are the most common complications encountered. Muscle weakness as a result of potassium deficiency may occur. With few exceptions, these complications are reversible by reduction of dosage or cessation of therapy. Concomitant testosterone therapy helps negate the effect of increased tissue catabolism.

CLINICAL AND LABORATORY PROCEDURES DURING THERAPY

Total circulating eosinophil counts should be obtained at from one-day to four-day intervals to make sure that an adequate initial decrease occurs. Subsequent rises in total circulating eosinophils are of no consequence. If clinical improvement does not accompany the decrease in total circulating eosinophils, the dosage should be increased temporarily. A record of the daily fluctuation in the body weight of the patient should be kept in order that accumulation of edematous fluid may be detected if it occurs.

Frequent determination of blood pressure is essential early in the course of therapy. After maintenance doses have been established, less frequent observations of blood pressure may be made.

Blood sugar determinations should be carried out at bi-weekly intervals until maintenance dosage has been established, and less frequently thereafter.

Observations for clinical signs of masculinization, particularly in women, are of great importance. Signs of muscle weakness should be looked for as an indication of possible potassium deficiency. With prolonged use of either hormone, simultaneous administration of testosterone is desirable because the catabolic effects of both ACTH and cortisone can be blocked by testosterone preparations without interfering with the therapeutic effect of either hormone. Significant alterations in psyche should be watched for carefully. When either hormone is used as an adjunct in the treatment of specific infectious states, actual or potential, adequate chemotherapy is mandatory.

RHEUMATOID ARTHRITIS

Other observers[1, 2, 3, 6] have reported that in every case rheumatoid arthritis can be ameliorated to some degree with ACTH or cortisone. The authors' experience in ten cases gives further evidence to support this view. All the patients were found to require continued therapy. With cessation of treatment short remissions of varying duration occurred; also, temporary exacerbations were observed immediately after cessation of therapy.

Most patients received either ACTH or cortisone alone. The average initial dose of ACTH was 100 mg. daily, and of cortisone 300 mg. daily. The average daily maintenance dose of ACTH varied from 20 mg. daily for some patients to 40 mg. daily for others; for cortisone the average was from 50 to 100 mg. daily. Some patients received these agents alternately and some received them concomitantly. Certain theoretical advantages may result from giving both drugs together or alternately.

At the time of this report, cortisone had become difficult to obtain for patients not critically ill and for this reason maintenance therapy was stopped in some cases. Several of the patients had severe recurrences of symptoms and psychologic changes which were definitely detrimental. The psychologic trauma so induced was a major problem in several instances. It is concluded, therefore, that therapy with these agents in rheumatoid arthritis should not be instituted unless reasonable assurance exists that maintenance therapy can be continued for indefinite and prolonged periods, both from the medical and economic standpoints.

ALLERGIC DISEASES

Asthma. In bronchial asthma these agents were of most value in the treatment of status asthmaticus. Indeed, in some cases use of the hormones was probably life-saving. They were also of definite value in epinephrine-fast and aminophyllin-fast patients,

and helped in producing remissions in long-standing cases resistant to other forms of therapy. The duration of relief varied; usually it was only temporary for patients who had had the disease for a long time.

In some patients with seasonal pollinosis, adequate courses of therapy induced remissions for an entire season. Two patients in this series had severe complicating pulmonary emphysema. Symptoms related to the emphysema did not improve under maximal therapy. Average doses for patients with bronchial asthma approximated those used in rheumatoid arthritis.

Atopic Dermatitis. As in bronchial asthma, both ACTH and cortisone were useful in alleviating symptoms of atopic dermatitis. Indications for use of the agents include resistance to conventional therapy, severe exacerbation, and anticipation of a prolonged period of disability. In the latter circumstances the agents may be given in hope of inducing early remission.

In several cases acceleration of eczema was observed after therapy was stopped. With parenteral administration of these agents in patients with atopic dermatitis, deep abscesses have been produced despite meticulous efforts to sterilize the skin prior to injection. It is believed that such abscesses result from deep-seated chronic infection of the skin.

Urticaria, serum sickness and drug sensitivity. In urticaria, serum sickness, and for control of symptoms of drug sensitivity, short courses of relatively low dosage were dramatically effective. It is the authors' belief that drug reactions constitute one of the prime indications for employment of these substances. It has also been observed that when strong psychogenic factors were present and possibly contributory in the production of urticaria, resistance to treatment was more pronounced.

Contact Dermatitis. Two patients with poison oak dermatitis experienced prompt and dramatic relief, one with ACTH alone, the other with cortisone. In the patient treated with ACTH, dermatitis was complicated by hypertension and acute nephritis, both of which disappeared within four days after institution of therapy and did not recur.

Vasomotor Rhinitis. Two patients were treated. Response was poor in both cases.

MISCELLANEOUS SKIN DISEASES

In treatment of miscellaneous skin diseases, the most dramatic response was observed in a single case of pemphigus. At the time of institution of treatment the patient had been hospitalized for several months, had been found resistant to many forms of therapy, and was near death. ACTH was used initially. Adequate doses produced prompt relief of symptoms. After three months of therapy ACTH was discontinued with resulting severe exacerbation. On resumption of ACTH therapy, it was found that the patient had become resistant to hog ACTH and to cortisone. However, the use of beef ACTH gave excellent results. After a short period ACTH was discontinued and cortisone substituted. Later ACTH in oil was used in place of cortisone. A year after the institution of therapy, the patient was entirely asymptomatic with small daily doses of cortisone.

In a case of scleroderma, moderate improvement in the skin lesions was observed. In this case a severe psychotic reaction necessitated discontinuance of therapy. One patient with dermatomyositis was treated with ACTH with partial relief of pain and partial clearing of skin lesions. During therapy a previously suspected peptic ulcer perforated, but in view of atypical symptoms, operation was delayed approximately 18 hours. The effect of ACTH in masking symptoms was considered a major factor in delay in diagnosis. Upon exploration, perforation of a duodenal ulcer was observed and there was extensive peritonitis.

Two cases of psoriasis were treated, one with ACTH and cortisone concomitantly, the other with cortisone alone. Both patients had dramatic and prompt relief of symptoms and dramatic reduction in severity of skin lesions but continuous treatment was necessary.

BURNS

Two patients with severe burns were treated. One patient with second and third degree burns involving approximately 50 per cent of the body surface was given ACTH and cortisone in small doses over a six-day period. The patient lived. In the second case, second and third degree burns involved 65 per cent of the body surface. ACTH and cortisone were also employed in small doses over a four-day period. The patient died of pulmonary edema on the sixth day.

DEMEROL ADDICTION

Both agents were highly effective in the control of withdrawal symptoms due to Demerol® addiction in three cases. Symptoms were relieved within 24 hours after therapy was begun. Full doses were employed over periods averaging ten days. At last report two of the patients had remained symptom-free for over two months. The third patient, who had been taking 1,200 to 2,000 mg. of Demerol daily, stopped use of the drug within 24 hours after institution of ACTH therapy. Some three months later the patient was being given 40 mg. of ACTH daily and there were no withdrawal symptoms.

LYMPHOMA

One case of monocytic leukemia, one of chronic lymphatic leukemia, and two of Hodgkin's disease were treated.

The patient with monocytic leukemia had relief of symptoms (as previously reported[5]) and peripheral blood and bone marrow remained normal for almost six months. However, with reappearance of abnormal cells in the peripheral blood and bone marrow, large doses of ACTH were resumed. Death occurred from spontaneous rupture of the spleen nine months after institution of therapy.

Full doses of ACTH and cortisone over a ten-week period were of no benefit in a case of chronic lymphatic leukemia.

Seven days of ACTH therapy in full doses was of no benefit in a terminal aggravation of Hodgkin's disease in one patient.

REGIONAL ILEITIS AND ULCERATIVE COLITIS

In one case of long-standing regional ileitis, full doses of cortisone brought about prompt and dramatic relief of symptoms within a three- to four-day period. At last report the patient had been free of symptoms for four months with a total daily maintenance dose of 37.5 mg. Reduction of the dose below that level resulted in return of abdominal discomfort. One patient with ulcerative colitis treated with average daily maintenance doses of cortisone was not benefited. Another patient with ulcerative colitis of long standing received ACTH during an exacerbation with definite and dramatic shortening of the period of exacerbation in comparison with previous episodes.

HYPOGLYCEMIA

Two patients with hypoglycemia were treated. One had excellent response with the continuous use of cortisone over a five-month period. With the use of ACTH and cortisone concomitantly for one month a good immediate but poor late response was obtained by the second patient.

GOUTY ARTHRITIS

One patient with gouty arthritis had good response with the intermittent use of ACTH and cortisone over a four-month period.

ACUTE INFLAMMATORY DISEASE OF THE EYE

A patient with acute iridocyclitis was treated with ACTH over a seven-day period. The result was excellent and there was no recurrence.

ACUTE (NON-SUPPURATIVE) THYROIDITIS WITH EXOPHTHALMOS

A patient with acute thyroiditis and exophthalmos was treated intermittently for a period of one year with ACTH and cortisone with good immediate but only fair late response.

MULTIPLE MYELOMA

One patient with multiple myeloma was treated for eight weeks with ACTH with no appreciable benefit.

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Use of the Rocking Bed to Augment Ventilation in Patients with Poliomyelitis

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SUMMARY

As the first step in an attempt to clarify criteria for use of the rocking bed rather than the respirator as an aid to breathing for patients with weakness of respiratory muscle function caused by poliomyelitis, ventilation studies were done on seven patients with pronounced weakness or paralysis of the respiratory muscles. Average tidal air volume was considerably less when the patient was on the rocking bed than when he was in the respirator. Since the tidal air volume with the patient on the rocking bed represents the maximum that can be produced with the apparatus, whereas the volume in the respirator represents the patient's usual tidal air and the respirator is capable of a greater volume if necessary, it is apparent that in cases of complete paralysis of the respiratory muscles the respirator has a large margin of safety, the rocking bed none.

From clinical observations made on 51 patients who were put upon the rocking bed—23 of them early in the course of the disease and 28 after they had been ill three months or more—it was concluded that the rocking bed is contraindicated for patients who are febrile and in whom the disease is progressing rapidly, and for those with atelectasis or urinary or pulmonary infection. It must be used with extreme care in the case of patients early in the course of the disease who are not tracheotomized, because of a tendency toward increased accumulation of mucus and the danger of atelectasis.

General guides were developed with regard to use of the rocking bed for patients with post-acute poliomyelitis, and somewhat different rules were drawn for use of the apparatus in cases in which there is a chronic respiratory problem.

The rocking bed will give artificial respiration in cases of respiratory weakness, but will not provide enough tidal air for the patient with paralysis of the muscles of respiration.

IN 1932, Eve[3] reported the use of a rocking stretcher for resuscitation. The patient was tilted from head to foot about 30° each way at a rate corresponding to that of natural respiration. The artificial respiration thus produced was sufficient to overcome pronounced respiratory distress and inadequacy. Eve reported using this method in two cases. In one case the patient was a small girl with post-diphtheritic paralysis of the diaphragm, and respiration was maintained for two or three days until there was adequate return of function in the diaphragm. Since that time, Eve has advocated the tilting stretcher for use in resuscitation, especially of the drowned, with tilting ranges up to 45° each way. The method appears to be more effective[1, 4] than those of either Schaefer or Silvester.

Since Eve's report in 1932, the rocking principle has been used in the treatment of peripheral vascular diseases.[8] The rate of motion of the Sanders bed, as well as its tilt, is much less than is necessary to produce any appreciable ventilation.

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Recently Wright[9] and Lenarsky[6] have advocated the use of the rocking bed in poliomyelitis with complicating respiratory insufficiency to aid in ventilation as well as to improve circulation and muscle function. A visit by Dr. Wright to the Los Angeles County Hospital and to the Rancho Los Amigos in 1949 stimulated the authors' interest in the use of the rocking bed in poliomyelitis. It is the purpose of this report to describe experience and experiments with the apparatus and to give criteria for its use based upon knowledge of the deficiencies of respiration as observed in the large number of cases of this type in Los Angeles County during recent years. The report deals primarily with the problem of inadequacy of ventilation. It does not attempt to establish the effect of the bed on circulation and muscle function.

TIDAL VENTILATION MEASUREMENTS

The effect of the rocking bed on breathing depends on the shifting of the abdominal contents that results from alternately lowering and raising the head of the patient. This shifting rhythmically elevates and depresses the diaphragm and consequently causes an appreciable tidal exchange of air. The effectiveness of respiration thus produced can be

evaluated by measuring the tidal air volume. It is probably impossible to measure this volume in the subject while he is awake or even during narcosis as long as the respiratory center can have any effect on breathing. The importance of this factor has been emphasized by Henderson.[5] To overcome this, Macintosh and Mushin[7] rocked two deeply narcotized subjects while spirometric measurements were made. One of the subjects was 140 pounds and the other 182 pounds in weight. With a tilt of 30° each way, a total of 60°, and a rate of 10 per minute, the tidal air values were 240 cc. for the smaller patient and 570 cc. for the larger. With a tilt of 45° each way, a total of 90°, the values were 380 and 635 cc. respectively. It should be remembered that the subjects did not assist or hinder breathing.

To better evaluate the ventilatory capacity of the rocking bed, it was decided to make spirometric measurements on patients with practically complete paralysis of the muscles of breathing. It was felt that this study would give further information about the properties of the beds available for clinical use, not just for the normal subject, but for patients of the type for whom the bed is intended. It is hoped that the results of these determinations and the clinical observations in the therapeutic use of the bed will lead to practical criteria for the safe use of the rocking bed in ventilatory deficiency.

Two types of rocking beds were employed in this study. They consist essentially of the usual Gatch type springs mounted on a mechanism to produce rocking from head to foot at a rate corresponding to respiration. One type* pivots at the top and center of the mattress, a mechanism made possible by a special tracking design. The speed and degree of tilting are adjusted by remote control on a separate panel. The tilt may be varied from 0 to 22° each way, a total of 44°, and the speed to about 24 oscillations per minute. This is the type of bed used by Dr. Wright.

The other bed† has a compound pivot so that besides rocking from head to foot there is also a lurch which appears to contribute to its action. The rate of oscillations can be varied from 12 to 24 per minute. The total tilt is about 35°, but the effect on respiration is about the same as that of the McKesson bed because of the compound action. The total tilt can be varied but slightly; however, the relative dip of head or foot can be varied. The Painter bed is mechanically controlled and is a single unit.

Spirometric measurements were done with a commercial metabolism apparatus‡ which was converted by removal of the unidirectional air valves and the insertion of a ventilating fan in the closed air circuit. A few readings were done with a spirometer§ modified to make tidal air determinations.

Nine tidal ventilation readings were done on seven patients who were practically completely paralyzed, but who had been well otherwise and whose condition had been unchanged for many weeks. Two patients had zero vital capacity, one 30 cc., one 40 cc., and the other three about 100 cc. The meager ability of some of these patients to breathe depended on action of the accessory muscles in the neck, a factor which could be easily watched and discounted during testing. The tidal air was measured while the patient was in the respirator which was set at the pressure used for the patient day and night. It should be observed that these readings indicated fairly closely the need of the patient, since any prolonged excess or inadequacy of respiratory volume would be reflected clinically. Comparison of these volumes with those produced by the rocking bed would aid in the evaluation of the adequacy of ventilation by the rocking bed. Most of the patients were given intermittent positive pressure artificial respiration while being transferred from the respirator to the bed and until the bed was actually rocking.

The accompanying Table 1 shows the results of the spirometric tests on the paralyzed patients. Tests No. 1 and No. 2 (Table 1) were done on the same patient to compare the Painter and McKesson beds. The same rate was employed, the head Gatch attachment was elevated 8 inches in each case, and the knees rolled up the same distance. The McKesson bed was tilted to its maximum. The Painter bed was adjusted to tilt the same at the foot and head. Test No. 4 was done on an experimental model of the Painter bed. On this bed the patient lay entirely flat. Comparison of the results in tests 1, 2, 4, and 5 indicated that the two beds produced almost equal ventilation.

It should be noted that in no case did the rocking bed produce as much ventilation as the patient had been getting in the respirator. It is significant that about half of the subjects could not tolerate the bed for more than a few minutes. The average of tidal air in those cases was about 54 per cent of what the patients had been getting in the respirator, whereas those who did not complain of air hunger averaged 77 per cent of the respirator tidal air. The average tidal respiration in the respirator was considerably more than the average tidal air that the rocking bed could produce in this series—383 cc. as compared with 251 cc. These findings are in line with those of Macintosh and Mushin, cited previously, but it should be remembered that the tilt used in the present study was 20° as against 30° and 45° used by Macintosh and Mushin.

To effectively produce sufficient ventilation, the rocking bed should have a tilt of at least 20° each way, 40° total. Greater tilt may be advisable, but the patient tends to slide too much. The supine position seems the most practical for the patient who has impaired breathing due to muscle weakness, but Macintosh and Mushin made the interesting observation that 25 to 50 per cent greater ventilation was

* Respir-aid Rocking Bed, McKesson Appliance Company, Toledo, Ohio.

† Painter Rocking Bed, M. D. (Jack) Painter, manufacturer, 640 South Washington Avenue, Whittier, California.

‡ McKesson Basal Metabalor, McKesson Appliance Co., Toledo, Ohio.

§ The Collins Vitalometer, Warren E. Collins, Boston.

TABLE 1.—*The Ventilatory Capacity of the Rocking Bed*

Test No.	Case No.	Sex	Age	Vital Capacity (cc.)	Tidal Air (cc.) Respirator	Tidal Air (cc.) Rocking Bed	Make of Bed	Reaction to test
1	2	F	23	100	270	200	Painter	Well tolerated
2	2	F	23	100	270	180	McKesson	Well tolerated
3	9	F	35	0	410	160	McKesson	Air hunger in 3 minutes
4	16	M	25	100	390	330	Painter	Well tolerated
5	16	M	25	100	350	300	McKesson	Nausea developed
6	17	M	22	100	470	210	McKesson	Air hunger in 1 minute
7	18	M	35	0	350	250	McKesson	Well tolerated
8	27	M	26	30	500	400	McKesson	Air hunger in 1 minute
9	28	F	27	40	440	230	McKesson	Air hunger after 1 minute
Averages:				63	383	251		

produced on the rocking bed with the patient prone.

The bed frame should be of the Gatch type. The back rest should be rolled up, about 8 inches, the knees about 4 inches. The feet should be snug against the foot-board, and it may be advisable to use shoulder supports. It may also be necessary to support the knees with a strap so that they do not flex as the patient is rocked.

It may be desirable to start the bed rocking in small arcs and then rather quickly increase the degree of tilt to the maximum. The rate of the bed ranges from 14 to 20 per minute for an adult, depending upon the natural rate of the patient's respiration; 18 to 24 per minute for children depending upon age and natural rate of respiration. Frequently, however, the patient's natural respiratory rate is considerably faster than the optimal rate for respiration by artificial means, including the rocking bed.

The time on the bed should be gradually increased from day to day while the patient is observed for any ill effects, especially increase in mucus, chronic fatigue and drop in vital capacity.

Although the ordinary nursing procedures can be done with the bed in motion, it is more convenient to stop it for short periods if tolerated. This also applies to physical therapy, although the rocking motion may help movement in some instances.

CLINICAL EXPERIENCES

At first the rocking bed seemed to offer good possibilities and use of it was begun with considerable enthusiasm. However, the original enthusiasm proved dangerous in some instances.

Altogether during the period of this study 51 patients were placed on the rocking bed. Of these, 23 were at the Los Angeles County Hospital and 28 were at Rancho Los Amigos. They were placed on the bed because it was thought the procedure would aid in reestablishing normal respiratory function. Because of the physical set-up at the Los Angeles County Hospital it was usually necessary to try to transfer the patient from the respirator to the rocking bed permanently. At Rancho Los Amigos, on the other hand, the patient could be transferred back and forth as needed. (The patients at Rancho Los Amigos included those for ventilation measurements already discussed.)

Use of the rocking bed in the County Hospital for the care of patients with acute poliomyelitis was begun on August 2, 1949. During the period of this study 23 patients ranging in age from 3 to 45 years were treated on it for varying periods of time: 14 were males, of whom three were children, and nine were females, one a child. These patients may be divided into an "early" and a "late" group. The early group was composed of six patients who were placed on the rocking bed before or very shortly after being placed in the respirator in the hope that the bed would give them sufficient assistance in breathing that the respirator would be unnecessary. The late group included 17 patients who were placed on the rocking bed ten days or more after being put in the respirator. In addition, three of the patients in the early group were again put on the rocking bed after they had been in the respirator for some time. They should therefore be considered as part of the late group, making a total of 20 in this group.

Of the six patients put on the bed early, only two escaped subsequent respirator care and these two might not have needed respirator care even without rocking bed assistance. One patient probably would have died had a respirator not been available and the three other patients did not do well while on the rocking bed.

When the rocking bed was used later in the disease with the patient afebrile, well stabilized and without complications, the time required to make him entirely independent of the respirator may have been slightly reduced in one-half of the 20 cases cited (see Table 2). However, eight of these patients were already spending three to six hours daily on a flat bed and one, No. 43, had almost full vital capacity before being placed on the bed, while another was spending 12 hours out of the respirator daily before the rocking bed regimen was inaugurated. Therefore, the time saved was probably minimal.

Three of the patients were placed on the rocking bed before ventilation studies were being made routinely. However, all had adequate exchange and good breathing patterns.

Five other patients had approximately one-third normal vital capacity or more. One, No. 46, was placed on the bed to drain a suppurative process in the chest.

On the other hand, five patients who were also afebrile and well stabilized did not improve while on the bed (Table 3) and consequently were returned to the respirators either just at night or around the clock, with subsequent increase in vital capacity.

Table 4 summarizes experience with six patients who were placed on the bed but in whom there developed complications which are described in case reports which follow. However, it is significant that two of the patients, Cases 31 and 36 (who, incidentally, did not do well on three occasions) had very low vital capacities. In two other cases, 32 and 35, increased mucus developed; in Case 35 this resulted in massive atelectasis and necessitated tracheotomy.

Of the 23 patients, ten complained of nausea on one or more occasions while on the rocking bed. This was apparently well controlled by Dramamine,® and only one patient was removed from the bed for this cause alone.

One patient delivered a fetus abortively, two required tracheotomy because of increased secretion of mucus, and one fell off the foot of the bed.

CASE STUDIES

A 25-year-old female patient (Case 29) was admitted on August 5, 1949, with a history of six days of illness with stiff neck, stiff back, fever and sore throat. Weakness of the right arm and shortness of breath had begun the day before admission. On admission it was noted the temperature was 100.4° F., the pulse rate 114, and respirations 40 per minute.

TABLE 2.—*Successful Use of Rocking Bed to Shorten Time of Transition from Respirator to Flat Bed*

Case	Sex	Age	Normal Vital Capacity (Calculated) (cc.)	Time Out of Respirator Before Put on Rocking Bed	Days Since Respirator Care Begun	Date	Time	Tidal Air (Bed) (cc.)	Vital Capacity at Rest (cc.)	Days on Bed	Reason for Removal
47	M	31	.....	20 min. thrice daily	18	.....	.....	Not recorded		7	Recovery
48	M	32	4,700	1 hr. twice daily	22	9-29-49	.....	300	900	6	Recovery
49	M	45	4,380	2 hr. thrice daily	64	12-28-49	.....	.....	1,650	12	Recovery
50	F	26	3,500	2 hr. thrice daily	36	10-12-49	.....	.....	1,150	8	Recovery
						10-20-49	.....	.....	1,400		
						10-26-49	.....	.....	2,600		
57	F	28	3,200	2 hr. thrice daily	16	10-21-49	.....	300	1,150	4	Recovery
						10-22-49	.....	300	1,690		
						10-25-49	.....	375	2,135		
						10-30-49	.....	.....	3,000		
40	M	11	.....	1 hr. thrice daily	14	.....	.....	No record		6	Recovery
30	M	31	.....	20 min. thrice daily	18	.....	.....	No record		7	Recovery
43	M	27	4,200	2 hr. thrice daily	10	3-30-50	9 a.m.	.....	3,150	1	Recovery
							3 p.m.	.....	3,150		
						3-31-50	1 p.m.	650	3,450		
							5 p.m.	650	3,600		
46	M	16	4,200	12 hr. daily		1-17-50	.....	.....	2,390	..	Recovery

TABLE 3.—*Unsuccessful Use of Rocking Bed to Shorten Time of Transition from Respirator to Flat Bed*

Case	Sex	Age	Normal Vital Capacity (Calculated) (cc.)	Time Out of Respirator Before Put on Rocking Bed	Days Since Respirator Care Begun	Date	Time	Tidal Air (Bed) (cc.)	Vital Capacity at Rest (cc.)	Days on Bed	Reason for Removal
37	F	29	3,300	4 hr. twice daily	14	11-11-49	.....	400	1,150	4	No increase in vital capacity. Respirator at night, flat bed during day.
38	F	19	3,200	5 hr.	30	12-10-49	.....	450	1,950	2	Vital capacity dropped to 1,700. Back in respirator except 5 hr. daily on bed.
39	M	22	4,900	3 hr. thrice daily	66	11-16-49	.....	400	1,025	21	Discharged in respirator. Needed respirator at night.
41	M	33	4,560	90 min. thrice daily	39	8- 8-50	8 a.m.	.....	2,050		Respirator at night.
							4 p.m.	.....	1,500		
						8- 9-50	8 a.m.	.....	2,600		Respirator at night.
							4 p.m.	.....	1,900		
						8-12-50	.....	.....	1,800	3	Chest pain.
						8-13-50	8 a.m.	.....	2,175		
						8-14-50	8 a.m.	.....	1,950		Fever, increased pulse and respiration rate. Returned to respirator.
42	M	17	4,500	2 hr. thrice daily	10	10- 7-49	8 a.m.	.....	1,100		Drop in vital capacity. Returned to respirator.

TABLE 4.—*Development of Complications in Well Stabilized Patients Placed on Rocking Bed*

Case	Sex	Age	Normal Vital Capacity (Calculated) (cc.)	Time Out of Respirator Before Put on Rocking Bed	Days Since Respirator Care Begun	Date	Time	Tidal Air (Bed at Rest) (cc.)	Vital Capacity (Bed at Rest) (cc.)	Days on Bed	Reason for Removal
31	F	21	3,100	45 min. thrice daily	18	10- 5-49	.....	275	650		Fatigue.
						10- 6-49	8:00 a.m.	.....	500	1	
						10- 6-49	3:00 p.m.	150	450		
32	F	29	3,000	30 min. thrice daily	21	10- 6-49	.....	400	950	3½ hr.	Increased mucus.
				45 min. thrice daily	26	10-11-49	8:30 a.m.	350			
							3:30 p.m.	275	925	6 hr.	Increased mucus.
33	F	12	.....	15 min. thrice daily	17	.....	.....	No record		9 hr.	Increased pulse.
34	M	7	.....	15 min. 4 times daily	21	.....	.....	No record		14 hr.	Nausea, dizziness, fatigue.
35	M	26	4,900	90 min. thrice daily	14	10-31-49	6:00 p.m.	.....	1,000	3¾ hr.	Increased mucus; tracheotomy.
36	M	27	4,800	.....	33	9- 6-50	.....	.....	350	1 hr.	Breathing 2 to 3 times rocking bed rate.
				30 min. thrice daily	54	9-27-49	9:00 a.m.	200	350	30 hr.	
							9:00 p.m.	75	150		Could not coordinate with rocking bed.
						9-28-49	9:00 a.m.	200	350		
							4:00 p.m.	75	200		

The patient was apprehensive and had pronounced nuchal rigidity. There was moderate spasm and weakness of both upper extremities. The intercostal muscles and diaphragm were weak. The spinal fluid contained 338 cells per cu. mm., all lymphocytes, and the reaction to a Pandy test was 2 plus. At the time of admission the patient could swallow water but shortly thereafter began to have difficulty in doing so. She was placed on the rocking bed at a rate of 18 to 20 per minute about 2 p.m., August 5. At that time the pulse rate was 130, respirations were 39 per minute, and oxygen was being given by nasal catheter. At 8 p.m. the pulse rate was 120 and respirations were 36 per minute. Two hours later the pulse rate was 112 and respirations 28 per minute. It was noted also that the patient slept for very short intervals during the night and in the morning she stated that she was very tired. The following evening the patient began to vomit, the pulse became rapid and faint and the blood pressure could not be measured. At 11 p.m. she was placed in a respirator where she remained overnight. The patient had some difficulty in coordinating with the respirator and the following morning, August 7 at 10:30, she was transferred back on the rocking bed. At this time the pulse rate was 80 and respirations 26 per minute. The rocking bed was running at 18 per minute and the patient finally coordinated with it after an hour or so. On August 9, the rocking bed was stopped for 30 minutes for meals and nursing care, and by August 12 the patient was rocking only from 8 p.m. to 6 a.m. On August 14 the bed was stopped entirely and on August 16 the patient was transferred to a regular bed. A two-and-one-half-month fetus was aborted on the same day. The patient was discharged on August 22, 1949, but with provision made for a standby respirator. At that time the intercostal muscles were weak, the diaphragm fair. There was rather pronounced weakness of both upper extremities and slight weakness of both lower extremities.

* * *

A 31-year-old man (Case 30) was put on the rocking bed on August 2, 1949, after he had been in the respirator four days. He became tired, apprehensive and cyanotic in 45 minutes on the rocking bed and was put back in the respirator. On August 16 he was placed on the rocking bed again, and six days later on a flat bed. (The patient actually falls into both of the previously defined groups, the "early" and the "late.")

* * *

A 21-year-old female (Case 31) was admitted and placed on the rocking bed on September 17, 1949 at 10:30 p.m. Vital capacity at the time was 800 cc. and tidal air 125 cc. The following day the vital capacity was 475 cc. but the patient remained on the rocking bed until September 21, 1949. At that time she was placed in the respirator at negative 18 pressure and ventilated at 450 cc. tidal air. On October 5, after two weeks in the respirator, the patient was again placed on the rocking bed. Tidal air volume at that time was 275 cc. and vital capacity was 650 cc. The following morning the vital capacity was 500 cc. and by 3 p.m. the tidal air had dropped to 150 cc. and the vital capacity to 400 cc. The patient was then put back into the respirator. The rocking bed treatment of this patient in both the early and late phases of the disease was therefore unsatisfactory.

* * *

A 29-year-old female (Case 32) had onset of symptoms on August 30, 1949, with gradually increasing paralysis. On September 14, 1949, partial facial paralysis and difficulty in swallowing were noted. The patient was placed on the rocking bed on September 14 at 1 p.m. and the vital capacity and tidal air volume were improving with the bed in motion. However, it was noted that by 5:30 p.m. there had been considerable deterioration and at noon the next day the vital capacity was 450 cc. The patient was placed in the respirator and tracheotomy was carried out. The patient remained in critical condition, with fainting spells and episodes of bradycardia, but by October 6 her condition was improved and the vital capacity was 950 cc. and the tidal air volume 400 cc. She was placed on the rocking bed for 3½ hours but was removed because of increased mucus. On October 10, the patient was again placed on the rocking bed, but six hours later was returned to the respirator.

* * *

In Case 33 the patient was placed on the rocking bed 17 days after she was placed in the respirator. She remained on the rocking bed for nine hours. Nausea occurred and Dramamine® was given, but the patient was returned to the respirator because of increase in pulse rate.

Twenty-one days after he had been put in the respirator the patient in Case 34 was placed on the rocking bed for 14 hours. He was removed from the bed because of nausea, dizziness and fatigue.

* * *

A 26-year-old male (Case 35) was admitted October 16, 1949, after five days of illness, with backache and headache and progressive weakness in the legs for two days, together with inability to cough. The spinal fluid cell count was 94 per cu. mm. and there was positive reaction to a Pandy test. As the condition of the patient deteriorated, he was placed in the respirator on October 17, 1949. The vital capacity at that time was 1,200 cc. By October 31, the patient was out of the respirator one and one-half hours three times daily and was considered a good candidate for the rocking bed. He was placed on the rocking bed at 6 p.m., and at 9:45 p.m. it was noted that there was considerable accumulation of mucus in the trachea. The patient became tired in unsuccessful attempts to cough it up. He was immediately placed back in the respirator. On the following morning it was noted that vital capacity had dropped to 750 cc. and that the breath sounds were absent over the entire left lung. The patient complained of pain in the left side of the chest. In x-ray studies atelectasis of the entire left lung was noted. The same morning laryngoscopy and bronchoscopy were carried out and a large amount of mucus was removed. Two days later, on November 3, the patient became cyanotic with a pulse rate of 140 and with gasping respiration. Bronchoscopy and tracheotomy were carried out and a good deal of mucus was brought up. With positive pressure and aerosol treatment the patient began to improve. He was permitted out of the respirator 15 minutes four times daily for nursing care only. The patient was discharged in the respirator December 2, 1949, to Rancho Los Amigos. At the time of discharge the vital capacity had returned to 1,070 cc. and the patient was permitted out of the respirator 30 minutes four times daily.

* * *

Case 36. The patient was placed in the respirator on August 4, 1949. On September 6, 1949, he was placed on the rocking bed. After one hour he was put back in the respirator as he consistently breathed two to three times the rate of the bed. However, it is interesting to note that at the time the vital capacity was approximately 350 cc. Another attempt was made to put this patient on the rocking bed September 27 (see Table 4). Thirty hours later the vital capacity was 200 cc. and the tidal air volume was 75 cc. and the patient was returned to the respirator.

* * *

Case 37. A 29-year-old female was admitted September 27. Tracheotomy was carried out and she was placed in a respirator. At that time the vital capacity was 400 cc. and the following day it was 200 cc. The patient began to improve and by November 11, when the vital capacity was 1,150 cc. she was out on a bed four hours twice daily.

The patient was put on the rocking bed to rock alternate hours until 8:00 p.m. and then rock all night. Dramamine® was prescribed. The second day she rocked at night but not during the day, a routine which was continued until November 15. It was then decided at a staff conference that since the vital capacity had not increased materially, the patient would be returned to the respirator for three nights and be permitted to be on a flat bed during the day. This was done and at the end of three days the vital capacity was 1,520 cc. The patient was then left in the respirator for another four nights and the improvement was maintained. She was then placed back on the rocking bed at night until December 5. At that time the vital capacity was 1,600 cc. or approximately 50 per cent of normal and the patient was permitted to sleep on a flat bed with no return to the respirator.

* * *

Case 38. The patient was placed on the rocking bed one month after she had been put in a respirator. At this time the vital capacity was 1,950 cc. However, with the patient on the rocking bed the vital capacity dropped and it was necessary to put her back in the respirator at night. Two days later, on December 20, she was returned to the respirator during the day also because it was felt that improvement had not continued. At the time of discharge the patient was spending five hours a day on a poliomyelitis bed and the rest of the time in the respirator. The vital capacity was 1,700 cc.

* * *

Case 39. The patient, a 22-year-old male, was first placed in the respirator on September 11, 1949. On September 22, he was placed on the rocking bed. Vital capacity at that time was 500 cc. By September 27 at 8:00 a.m. the patient had become irrational and confused and he was returned to the respirator at 4:00 p.m. Vital capacity then was 300 cc. On November 16, the patient was again placed on the rocking bed. At this time vital capacity was 1,025 cc. and tidal air volume 400 cc. After two days he was put in the respirator at night and on the rocking bed during the day, a routine which was followed until the patient was transferred to a naval hospital, Dec. 6, 1949. Vital capacity at the time of discharge was 1,000 cc.

* * *

In Case 46 the rocking bed was used to aid in chest drainage. A 16-year-old boy was placed in the respirator Nov. 16, 1949. There was pronounced involvement of the third, fourth, sixth, seventh, ninth, tenth and eleventh cranial nerves. Suppurative pulmonary disease and right lower lobe atelectasis and pneumonia developed, and the rocking bed was used to agitate the secretions and to place the patient in Trendelenburg position for a short period several times daily so that satisfactory drainage could be obtained. Eventually the rocking bed was substituted at night for the respirator, but at the time it was first used the patient had a vital capacity of 2,200 cc. and was out on a flat bed for 12 hours daily.

* * *

Case 41. A 33-year-old male was placed in a respirator July 1, 1950. On August 8 he was out of the respirator one and one-half hours three times daily and doing well. He was placed on the rocking bed at 8:00 a.m. on August 8. Vital capacity then was 2,150 cc. When the patient was returned to the respirator at 4:30 p.m., vital capacity was 1,500 cc. After a night in the respirator vital capacity rose to the previous level and during the following day on the rocking bed it decreased only 200 cc. On Aug. 12 the patient complained of pain in the chest. The vital capacity was 1,800 cc. After 24 hours in the respirator, vital capacity was 2,175 cc. and the chest pain was gone. The patient then was put back on the rocking bed and permitted to rock for 24 hours. At 8 a.m. the temperature was 102.6°F., the pulse rate 134 and respirations 24 per minute, and vital capacity was 1,950 cc. The patient was nauseated. At noon he was put back in the respirator. The fever continued.

The rocking bed was employed as a treatment procedure for 23 patients with chronic poliomyelitis at Rancho Los Amigos. Five of the 23 could not remain as much as 10 minutes out of the respirator. Sixteen patients were able to remain out of the respirator at least several hours but had to be returned

for the night. The remaining two returned to the respirator for occasional rest.

The 23 patients will be considered in three groups. The first consisted of five patients who had a short tolerance time out of the respirator and were put on the bed for periods of up to four hours. In the second group were nine patients who were able to breathe without assistance for at least several hours but still had to sleep in the respirator. In these cases the question was not whether there was adequate ventilation while rocking, but whether there were any possible undesirable side effects. In the third group there were nine patients who tried to sleep on the rocking bed after they had tried the bed during the daytime. They would otherwise have had to sleep in a respirator.

Table 5 gives data on the five patients in the first group. In all of these cases the patient was put on the rocking bed for short periods once daily and the time was gradually increased to the maximum period indicated. The inclination of rocking was 18 or 22 degrees depending on the bed used, although with the first patients the angle may have been somewhat less. The head section of the Gatch frame was raised about 8 inches and the knee section broken about 4 inches. The rate of oscillation varied from 16 to 20 per minute depending on the natural respiration rate of the patient and on the subjective response.

In Cases 2, 5 and 10 the patients tolerated the bed from one to four hours daily but then had to be returned to the respirator because they usually complained of fatigue, although naturally the exact time varied with the general vitality of the patient. These patients had no diaphragm or intercostal strength and it was noted that they assisted the rocking bed action with the use of the accessory muscles in the neck. Hardly ever did these patients nap on the rocking bed. In Case 9 the length of time the patient spent on the rocking bed was gradually increased to about one hour. It was necessary to give her supplementary oxygen. After two or three weeks it was noted that there was a gradual decline in general strength, that the patient was not able to tolerate physical therapy as well as previously and that it became necessary to increase the amount of oxygen. In Case 11 the course was similar. Accumulation of mucus increased and a respiratory infection developed. It was felt that the rocking bed was contraindicated in these cases, although shorter periods might have been tolerated. While out of the respirator and on the bed, these patients received more physical therapy than they had been accustomed to, and this may have contributed to the intolerance. The use of the bed was stopped in the other cases because of reasons other than undesirable effects. In Case 10 the patient was sent home, there to remain in a respirator full-time.

Nine of the patients who were given rocking bed treatment had considerable independence of breathing; all of them could be out of the respirator for several hours (Table 6). With them, it was not at all a question of adequacy of ventilation when on the rocking bed. It should be noted that in one case in this group increased mucus in the trachea was a complication. Treatment periods were one hour once daily.

If the rocking bed could be substituted in cases in which the respirator is required only for sleep, a possible saving in patient care, a more natural situation for sleep, improved morale, and other possible benefits might be expected. With this in mind, nine patients who already had shown good tolerance to rocking during waking hours were considered good candidates for sleeping on the rocking bed. All of the nine patients except one (Case 20) had been using the rocking bed, while awake, for weeks. In most cases the period of rocking was increased to five or six hours into the sleeping hours before the patient was permitted to sleep on the bed through the night. The patients were observed closely for any signs of loss of sleep, progressive fatigue and drop in vital capacity.

Table 7 summarizes the observations in these cases. It should be noted that the vital capacity of these patients was 300 cc. or more at the beginning of this study. The patients could usually sleep well even though most breathing was largely by neck accessory muscles. With a small amount of diaphragm action, other conditions being equal, it would be expected that sleeping on the rocking bed would be much easier. This is in accord with repeated clinical observations on patients who try to sleep without the aid of artificial respiration. All of the patients except one (Case 20) would have needed the respirator for sleep if it had not been for the aid produced by the rocking bed.

One patient (Case 7) required the use of the res-

TABLE 5.—*Rocking Bed Tolerance with Short Tolerance Out of Respirator*

Case	Sex	Age	Onset	Date Rocking Bed Started	Date Rocking Bed Stopped	Tolerance Out of Respirator	Maximum Tolerance on Rocking Bed	Stabilized Vital Capacity (cc.)	Remarks
2	F	23	8-10-48	8-22-49	5-50	5 min.	4 hr.	100	Patient transferred
5	F	35	6-25-48	11- 2-49	5-50	5 min.	1 hr.	100	Patient transferred
9	F	35	11-15-48	11- 2-49	12-19-49	3 min.	1 hr.	0	Did not tolerate
10	M	25	11-15-48	11- 2-49	1- 5-50	2 min.	1 hr.	100	Discharged home
11	F	27	11-15-48	11- 2-49	12-16-49	10 min.	1 hr.	250	Did not tolerate

TABLE 6.—*Rocking Bed Tolerance with Long Tolerance Out of Respirator*

Case	Sex	Age	Onset	Date Rocking Bed Started	Vital Capacity (cc.)	Remarks
1	F	37	8- 2-48	8-22-49	300	No undesirable effects—still uses bed.
3	F	33	10- 9-48	11- 9-49	300	No undesirable effects—still uses bed.
4	F	28	9- 4-48	11- 9-49	750	No undesirable effects—discharged February 1950.
8	F	38	9-15-48	11- 9-49	900	No undesirable effects—now once weekly.
13	M	5	10-14-48	8-49	400	No undesirable effects—stopped December 1949.
14	F	27	7-14-48	8-49	1,000	No undesirable effects—stopped December 1949.
15	M	42	11-13-48	8-49	700	Tried only few times—patient did not like it.
19	F	21	9-28-48	4- 7-50	350	Tolerated—but increased mucus.
23	M	16	7-31-48	11- 2-49	600	No undesirable effects.

TABLE 7.—*Substitution of Rocking Bed for Respirator When Respirator Used Only at Night*

Case No.	Sex	Age	Onset	Date Rocking Bed Started	Vital Capacity (cc.)	Date Rocking Bed Stopped	Vital Capacity (cc.)	Breathing Pattern	Remarks
6	M	17	8-28-48	3-20-50	470	Continued	600	Neck chiefly, some chest, no diaphragm	Sleeps well on rocking bed
7	F	31	7-11-48	1-12-50	300	1-26-50	400	Neck accessories only	Slept poorly, very tired
12	F	34	11-11-48	12- 2-49	400	12-23-49	1,400	Weak chest and diaphragm; some neck accessory action	Slept well but tracheal bleeding
20	M	18	3-20-50	5-31-50	2,000	6- 6-50	2,300	Good pattern, slight weakness	Transition from respirator to bed
21	M	22	11-18-49	7-10-50	1,350	10-20-50	1,350	Weak diaphragm and chest, uses neck	Transition from respirator to bed
22	M	19	7-22-48	11- 7-49	400	1-13-50	400	Uses neck only	Slept well; discharged with respirator
24	F	33	11- 4-48	2-28-50	700	5- 9-50	700	Weak diaphragm and chest, uses neck	Slept well; transition from respirator to bed
25	M	7	11- 8-48	5- 2-50	480	5- 8-50	480	Nearly all neck accessory action	Slept well but temporary complications
26	M	14	10-10-48	1-16-50	400	Continued	600	Nearly all neck accessory action	Sleeps well

pirator with a very high negative pressure (35 cm. of water). This was sufficient to produce over one liter of ventilation. It is plain that if the patient were to breathe this amount of air continuously at each breath, alkalosis and tetany would soon develop. This was prevented by the patient by throttling all but every third or fourth breath so that on the average she would breathe the proper amount. The respirator pressure used in this case is difficult to maintain and with it there is a possibility of damage to the cardiorespiratory system. For this reason attempt was made to break this peculiar breathing mechanism by having the patient sleep on the rocking bed. The patient was able to get some sleep, but she became progressively insomnic and signs of exhaustion appeared. In spite of the poor clinical effect, the vital capacity increased. However, the rocking bed for sleeping was discontinued.

Although in Case 12 the patient slept well, tracheal bleeding of unknown origin developed while the rocking bed program was being followed, so it was decided to discontinue the procedure.

In Cases 6, 20, 21, 22, 24, 25 and 26 the patients appeared to tolerate the rocking bed well for sleeping at night; and two of these patients (Cases 6 and 26) are still using it. In Cases 20, 21 and 24 the bed was used to advantage in weaning from the respirator. In Case 22 the rocking bed had to be discontinued when the patient was discharged home where he uses a tank respirator. In Cases 25 and 26 the patients had to return to use of the respirator temporarily because of complications apparently not related to the rocking bed. In Case 25 use of the rocking bed was discontinued because it had to be removed from the ward.

About half of these nine well stabilized patients with chronic poliomyelitis had an upward trend in vital capacity while on the rocking bed.

DISCUSSION

These clinical observations on patients with weakness of respiratory muscles, as well as accepted physiological principles point to the concepts which should be considered in the use of the rocking bed when there is appreciable weakness of the muscles of respiration.

Ordinary breathing consists of the tidal ventilation of air in and out of the lungs. The ventilation per minute is determined by the rate and depth of breathing. This volume is precisely controlled by the respiratory center which in turn may be influenced directly or reflexly by various factors such as oxygen and carbon dioxide tensions of the blood plasma, blood bicarbonates and pH, certain hormone-like substances, the Hering-Breuer reflexes and a number of drugs. Pulmonary ventilation has two important functions: One is to maintain the proper oxygen tension of the blood; the other is to aid in maintaining the proper blood pH. Hyperventilation produces blood alkalosis (respiratory alkalosis) because the carbon dioxide is worked out of the lungs but no appreciable increase in blood oxygen tension or increase in oxyhemoglobin saturation occurs. Inadequate ventilation produces relative acidosis (respiratory acidosis) resulting from an accumulation of carbon dioxide and a decrease in blood oxygen tension associated with a decrease in the oxyhemoglobin saturation. Deficiency of ventilation does not decrease the oxygen requirements of the tissues except in the terminal stage of asphyxiation (anoxia) and possibly in chronic anoxia which is sufficiently prolonged and intense to produce tissue deterioration.[5] In the presence of a normal cardiorespiratory system, adequate strength of the respiratory muscles, a normal regulatory system and adequate oxygen, the oxygen supply to the tissues is ample over a wide range of conditions and the blood pH is maintained within narrow limits (pH 7.35 to pH 7.45). In the presence of weakness of the respiratory muscles this system may break down, although a certain amount of compensation—increase in pulse rate and in the bicarbonate content of the blood—takes place. In the presence of good nutrition there may be an increase of hemoglobin, but the tendency is toward anemia.

There is considerable clinical evidence that prolonged mild anoxia and exhaustion associated with pronounced weakness of the respiratory muscles in poliomyelitis will lead to general tissue deterioration especially of the brain and the gastrointestinal tract. This seems to result especially from inadequate exchange of oxygen and carbon dioxide during the sleeping hours. Some of these observations have been emphasized in a previous publication.[2]

The most important muscle of respiration is the diaphragm. Sudden bilateral phrenic nerve paralysis is very serious unless the patient is given adequate artificial respiration. The muscles that produce expansion of the lower chest function chiefly in preventing chest collapse when the diaphragm acts. The most automatic pattern of breathing is that carried out by the action of the diaphragm together with expansion of the lower chest. This is normally the chief component of what may be termed "unconscious breathing." The muscles that expand and raise the upper chest also take part in quiet breathing but to a lesser degree. If there is sufficient weakness of the diaphragm so that it cannot easily maintain the required ventilation, the muscles that expand and raise the chest increase in their action. If this action is inadequate, the accessory muscles in the neck in turn come into action and the muscles producing chest and abdominal compression may eventually assist breathing. Just which muscles are used depends on the required tidal air, on general and individual muscle strength, on the wakefulness of the individual and on habit patterns that have been developed.

If the patient has to depend to an appreciable degree on accessory muscles for quiet breathing, it is usually difficult for him to sleep, since "unconscious breathing" usually requires the use of the diaphragm and lower chest muscles. Such a patient may "subconsciously" use various accessory muscles during the waking hours and have sufficient ventilation. In a certain number of cases accessory patterns of breathing seem to become well linked to the respiratory center and become automatic "unconscious breathing," so that breathing with accessory muscles while asleep may be adequate. In such circumstances, however, great care should be taken lest the chronic effects of partial asphyxia develop because of inadequate muscle strength or insufficient automaticity. If accessory action is not well established for sleep, the cerebral and somatic functions may so deteriorate that the patient may even die unless he is given adequate artificial respiration, especially while sleeping.

Tests by the authors as well as those of Macintosh and Mushin indicate that the rocking beds that were used did not produce the tidal air required for quiet breathing in cases of complete paralysis. In contrast, the tank respirator is capable of producing about two times the basal tidal air required in most cases. Therefore, it appears that the rocking beds tested can be safely used during sleep only in those cases in which there is at least an appreciable amount of "unconscious" or automatic breathing, and during the waking hours only if the patient is able to sufficiently supplement the effect of the bed by subconscious effort without signs of fatigue or impairment.

CRITERIA FOR USE OF THE ROCKING BED

On the basis of the physiological concepts and clinical observation described in this report, the rocking bed can be used for the purpose of assisting respiration in cases in which there is weakness of the respiratory muscles. It should not be used during the febrile period of poliomyelitis, nor in the presence of secondary complications such as atelectasis, pneumonia, upper respiratory tract infection and urinary infection.

The rocking motion may cause motion sickness, as manifested by nausea and dizziness, especially if the bed is used soon after the occurrence of paralysis. Dramamine® is of value in the prevention of this complication.

It has been observed that the rocking motion tends to increase the amount of mucus in the respiratory tree, particularly during the first few hours, but the explanation is not clear. If the patient tends to have an increase in mucus as in respiratory infection and moderate bulbar involvement, the rocking bed may be contraindicated, especially in the absence of tracheotomy. Any patient when first placed on the rocking bed should be given individual nursing care and should be closely observed for increased mucus and possible occlusion of the bronchi.

The programs followed by the authors for placing patients on the rocking bed varied to accord with the facilities for special nursing care and in consideration of whether the patient was in an early stage of the disease or had had it for a number of months. Observations indicated that the following considerations and methods make for the best rocking-bed program for patients during the first few weeks after the febrile period:

1. The patient should be able to be out of the respirator at least one hour three times daily without the use of the accessory muscles and with no increase in pulse rate or other untoward reaction.

2. The vital capacity should be at least one-third of the normal standard, and there should be record of a consistent increase with at least one-half of the vital capacity due to diaphragmatic action, before a patient is considered for rocking-bed treatment.

3. When the patient is on the rocking-bed program, the vital capacity should be tested twice daily for several days, and daily thereafter. If it decreases, return to the respirator is indicated.

4. The daily schedule should begin with six to eight hour periods on the rocking bed, with the patient returned to the respirator at night. If there are no ill effects and the vital capacity does not decrease, the patient then may be permitted to sleep on the rocking bed.

Patients who in the early stages of the disease do not meet the criteria for being put on the rocking bed, may later do well with this treatment even though they then may have much lower vital capacity.

Between the eighth week and the eighth month, when muscle function is still returning, the patient ordinarily should not be permitted to use the accessory muscles of breathing. If during that period he is able to be out of the respirator for as much as 15 minutes at a time without using accessory respiratory muscles, the rocking bed can usually be well tolerated during the daytime, provided the time he spends on the bed is not too rapidly increased.

Some patients who need to use the accessory respiratory muscles because of moderate weakness of the diaphragm and intercostal muscles may do well on the rocking bed for short periods, but they should be closely watched.

If, after six to eight months, there appears to be no appreciable return of diaphragmatic strength, it is usually advisable to permit the patient to use the neck or other accessory muscles when he is out of the respirator. If it appears early that there is little likelihood that diaphragm function will improve, the period of trial may be shortened somewhat. A patient who has no return of chest and diaphragm muscles should develop the strength of the accessories. Usually if there is no weakness of the accessory muscles the patient is able to remain out of the respirator all day. The vital capacity in such a case should be at least one-tenth normal. Usually, however, a patient who depends upon the action of accessory muscles cannot breathe while asleep unless assisted by a respirator or rocking bed. It appears clinically in such cases that the respiratory center takes over during sleep with difficulty. Great care should be taken before such a patient is permitted to sleep on the rocking bed, since the bed only assists in the volume of breathing. It is important to follow the progress of the patient carefully with regard to general vitality, appetite, nutrition, mental alertness, vital capacity, and development of disturbing symptoms such as headache.

The following guides would seem to be applicable for use of the rocking bed for patients six months or more after onset of the disease — always with recognition, however, that they must be modified in event of development of certain side reactions such as nausea, vertigo, accumulation of mucus, and signs of fatigue, exhaustion and anoxia including changes in pulse rate, lassitude, loss of appetite and decrease in vital capacity:

1. If the patient has no vital capacity and cannot be out of the respirator more than three minutes, use of the rocking bed is not feasible.

2. If the patient is able to be out for more than three to five minutes, especially if there is fair function of the diaphragm, he can usually be put on the rocking bed for increasing times, up to several hours.

3. If the patient is able to be out several hours on his own strength, there should be no difficulty whatsoever in placing him on the rocking bed, for any desired time, during the waking hours.

4. If the patient is able to be out of the respirator all day without any difficulty, especially if vital capacity is over 10 per cent of normal and at least half of this is due to diaphragm action, then he should be able to sleep on the rocking bed. In some cases even patients who depend entirely on accessory muscles for breathing do well sleeping on the rocking bed. It is important that conversion to sleeping on the rocking bed be done gradually and that vital capacity be checked daily for the first two or three days. All patients, and especially those who depend on accessory muscle action, should be watched very carefully for signs of intolerance.

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Trisethylene-Imino-s-Triazine (Triethylene Melamine or TEM) in the Treatment of Neoplastic Diseases

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SUMMARY

Trisethylene-imino-s-triazine (triethylene melamine or TEM) produced minimal effects in inhibiting transplantable lymphoma and mammary adenocarcinoma in mice. In strain A mice, injection of the compound induced pulmonary tumors.

TEM was tried on 32 patients with neoplastic disease, including nine patients with Hodgkin's disease and five with lymphosarcoma and lymphatic leukemia. The therapeutic and toxic effects were similar to those observed with nitrogen mustard (HN2). Satisfactory remissions of up to three months were observed in Hodgkin's disease and lymphosarcoma following parenteral administration of TEM. It is the authors' impression that the remissions obtained with TEM were not as complete and did not last as long as those obtained with HN2.

TEM is effective by the oral route as well as parenterally, and produces much less emetic reaction than HN2. On the other hand, the chemotherapeutic range is narrower than that of HN2. Patients who do not respond to HN2 show no response to TEM.

TEM is a drug of some clinical usefulness in the same conditions and with the same general limitations and toxic effects as HN2. The ease of administration of TEM increases its hazards, and close clinical and hematologic observations are essential on patients receiving the agent.

THE discovery that certain nitrogen mustard compounds have ameliorative effects in Hodgkin's disease and related lymphomas[4] has led to the synthesis and biologic testing of a wide spectrum of related chemicals for their tumor-inhibiting properties. The investigations thus far have not uncovered agents which by clinical standards are clearly superior to methyl-*bis* (B-chloroethyl) amine (HN2) or methyl-*tris* (B-chloroethyl) amine (HN3). These powerful vesicants must be given directly into the blood stream, and they produce severe nausea and vomiting as well as occasional phlebothrombosis.

Chart 1.—Chemical structures of TEM.

A number of compounds related to the nitrogen mustards have been devised recently in England[7, 9] and the United States[3, 6] which appear to have effects similar to the nitrogen mustards but which have less emetic reaction and are effective when administered by the oral route. Among these compounds (Chart 1) is trisethylene-imino-*s*-triazine.

The present report deals with the laboratory and clinical investigations of trisethylene-imino-*s*-triazine.* This compound is more familiarly known as triethylene melamine or TEM, as it will be referred to hereinafter.

ANIMAL STUDIES

Toxic effects. Mice of strains A and C3H, three months old and weighing approximately 25 gm., tolerated doses of 0.04 mg. of TEM dissolved in water or saline solution and injected intraperitoneally or intravenously. Approximately half of the group of animals died within five days following doses of 0.1 mg. There was a precipitous drop in the number of circulating leukocytes, and a moderate drop in the number of platelets within four days following

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*The compound was made available for this study in November 1949 by Dr. Frank L. Rose of the Imperial Chemical Industries, Manchester, England. Dr. M. L. Crossley of the American Cyanamide Company supplied tablets of the material for oral use.

the administration of 0.1 mg. In histological examination of the tissues of the mice, the following phenomena were observed: Vascular engorgement of the viscera, disappearance of lymphocytes with atrophy of Malpighian corpuscles in the spleen, loss of cells from the follicles of lymph nodes, pronounced decrease in the cellular elements of both series in the bone marrow, and necrosis of the germinal epithelium of the testes.

Effect on tumors. The effects of TEM on tumor growth were investigated in strain A mice implanted with a transplantable lymphoma, and in strain C3H mice bearing a transplanted mammary adenocarcinoma. The animals were given 11 daily intraperitoneal injections of 0.0025 or 0.005 mg. of TEM dissolved in water, for a total dose of 0.0325 mg. Six mice were sacrificed at 12 days and the weights of the tumors and of the carcasses were compared with those of six untreated animals. The lymphomas in mice treated with TEM weighed an average of 1.45 gm. (0.9 gm. to 2.1 gm.), whereas the untreated tumors weighed 3.2 gm. (2.7 gm. to 4.6 gm.). The effect on mammary tumors was much less pronounced; the tumors of the treated animals weighed 2.5 gm. on the average, whereas the untreated tumors weighed 2.9 gm. The total body weight of the animals was not affected.

The experiment was repeated with ten mice in the treated and untreated groups of each strain. The strain A mice with the lymphoma treated with TEM lived for an average of 36 days (29 to 38) whereas the controls died at an average of 33 days (29 to 37); the tumor obviously grew rapidly after the conclusion of the treatment. The strain C3H mice with mammary tumors treated with TEM lived an average of 31 days (22 to 51) whereas the untreated controls survived for 23 days (12 to 35). In all animals there was progressive growth of the neoplasm even while under active treatment with TEM, and all the animals died of the neoplastic growth.

Reported effects on other transplantable lymphomas, sarcomas and carcinomas in the mouse[3, 6] and on the Walker rat carcinoma[9] indicate more pronounced inhibition of tumor growth than was elicited in the present investigation.

Carcinogenic effect. It has been pointed out[11] that many chemical agents which have inhibitory effects on tumor growth also have carcinogenic properties. The nitrogen mustards, for example, induce pulmonary tumors in mice.[5]

TEM was administered intravenously to 20 strain A mice two months of age. The initial dose of 0.05 mg. in 0.1 cc. of saline solution was followed by two doses of 0.025 mg. at monthly intervals, for a total dose of 0.1 mg. Six additional mice received single intraperitoneal injections of 0.05 mg. Fifteen mice were maintained as untreated controls. The mice were sacrificed 18 weeks following the initial injection, and the lungs were examined for the presence of pulmonary tumors.

Of the 15 untreated controls, two had solitary pulmonary tumors. This incidence coincides with the 10 to 15 per cent incidence of spontaneous pulmonary tumors in strain A mice six to seven months of age.[10]

The six mice that received 0.05 mg. of TEM intraperitoneally had 2, 3, 0, 2, 1, and 0 pulmonary tumors, respectively, or an average of 1.3 tumors per animal. The 20 mice injected with 0.1 mg. intravenously had an average of 2.1 pulmonary tumors per animal; four mice had no tumors, four had single tumors, eight had two to three tumors, and four had four to six nodules in the lungs.

Four C3H male mice injected subcutaneously or intraperitoneally with 0.05 mg. of TEM were killed one year later. No tumors at the site of injection were found, but two mice had one and two pulmonary tumors, respectively.

It is concluded that TEM is carcinogenic for the pulmonary tissue of mice, and that its carcinogenic potency is of the same order as found for HN2 by Heston.[5]

CLINICAL STUDIES

Since February 1950, 32 patients with advanced neoplastic disease have received 60 therapeutic courses of TEM. Of the patients, 30 were treated at the Laboratory and two at Letterman Army Hospital.* The diagnoses in all cases were based on microscopic examination of at least one relevant biopsy specimen.

TEM is a white powder that is immediately soluble in water or in saline solution. Occasional samples of TEM contain granules or flakes which do not dissolve, indicating that polymerization has occurred and that the material should not be used. The compound is relatively stable in solution, and can be used for at least 24 hours if maintained in the refrigerator. For intravenous or intramuscular injection TEM is dissolved in sterile physiological saline, in concentrations of 1 or 2 mg. per cc.

For oral use, tablets of 5 mg. in a bland binder were employed. These were given with water, usually a half-hour before the noon meal.

Information regarding the patients and the treatment with TEM is given in Tables 1 and 2. There was no difference in toxic or therapeutic effects when the agent was given intramuscularly or intravenously, nor when the total dose was given in a single injection or in daily injections for three to seven days. The therapeutic dose or single course of TEM, if given intravenously or intramuscularly, is approximately 0.15 mg. per kilogram of body weight and should not exceed 0.25 mg. per kilogram of body weight. The agent should not be readministered until the hematologic status of the patient has returned to normal, which usually occurs within four to five weeks.

One patient (Case 19) with disseminated epidermoid carcinoma, primary in the nasopharynx, was injected intravenously with 0.5 mg. per kilogram of body weight and died on the 14th day showing hemorrhagic diathesis associated with pancytopenia.

*The staff of Letterman Army Hospital granted permission to use records on these two patients.

With oral medication, daily doses of 5 to 10 mg. for a total of 0.4 mg. per kilogram of body weight appear to be the safe upper limit for a single course of treatment. One patient (Case 4) with Hodgkin's disease received 0.9 mg. per kilogram of body weight during a course of two weeks, and hemorrhagic diathesis with petechiae, thrombopenia, severe leukopenia, and anemia developed. Repeated transfusions of whole blood, antibiotics, and other supportive measures were required.

Patients with lymphocytic leukemia appear to be extremely sensitive to TEM, and an initial parenteral dose of 0.05 mg. per kilogram of body weight, or 5 mg. orally, should not be exceeded until the effects of these lower doses are well established on the individual patient.

PHARMACOLOGIC EFFECTS

Immediate effects. In three cases study was made of electrocardiographic tracings, blood pressure, pulse and respirations during and for several hours following the intravenous administration of 0.1 mg. per kilogram of body weight. There were no significant changes. There were no general or local reactions to the agent within the first hour with any of the three routes of administration employed.

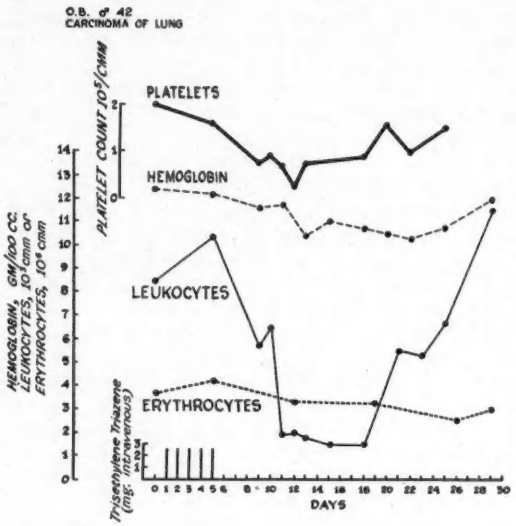
Local effects. In all but one patient, no serious local reactions occurred at the site of intravenous or intramuscular injection. Approximately one-third of the patients complained of some soreness at the site of intramuscular injection. In one patient (Case 15) with myelocytic leukemia, pronounced induration and inflammation occurred in the sites of intramuscular injection, and intravenous injection produced tenderness and redness along the course of the vein.

Gastrointestinal effects. Patients receiving over 0.2 of TEM per kilogram of body weight by intramuscular or intravenous routes experienced nausea for two to four days after completion of the course. Approximately one-third of these patients had one to four episodes of vomiting. The reaction was much less pronounced than that with HN2, and was usually delayed for four to six hours, as compared with the reaction to HN2, which usually occurs within an hour. With parenteral doses of 0.05 mg. per kilogram of body weight, or by oral route of administration, only mild nausea was encountered, unless the agent in a concentrated solution was injected rapidly into the vein. Diarrhea following treatment with TEM was noted in two patients receiving large doses of the agent.

Severe frontal headache, observed occasionally following HN2, was not observed in the 32 patients of this series treated with TEM.

Hematologic effects. The chief toxic effect of TEM is on the hematopoietic system. This effect is in every way comparable to the effects observed with HN2. Chart 2 illustrates the characteristic alterations observed on the peripheral blood picture of a patient with a bronchogenic carcinoma who received a dose of 0.25 mg. per kilogram of body weight.

Chart 2.—Characteristic effect of TEM on the cell count in peripheral blood. The patient with bronchogenic carcinoma (Case 21) received an intravenous course of 0.25 mg. per kilogram of body weight.



Within ten days there was a rapid decrease in the leukocyte and the platelet count, and a slower decrease in the erythrocyte count and hemoglobin value. In bone marrow aspirations at this time pronounced diminution in hematopoiesis, both of the white and red cell elements, was noted. Recovery from this depression began approximately three weeks after the drug was given.

With oral administrations, the hematologic depression was somewhat slower, particularly if the drug was administered at intervals of two or three days. The nadir of the leukocyte depression was usually observed in approximately two weeks and the count returned to normal within six weeks.

Other effects. In study of clinical and laboratory determinations before treatment with TEM and for as long as three months following treatment, no other major toxic effects that could be attributed to TEM were noted. In repeated examinations of the urine no significant changes were observed. Liver function, as measured by blood bilirubin, thymol turbidity, bromsulfalein retention, and cholesterol fractions, was not definitely changed. In one patient with Hodgkin's disease with jaundice, icterus was reduced following TEM therapy. Serum non-protein nitrogen, serum proteins, sodium, potassium and chloride were determined before and after treatment. There was no change in these factors. The uric acid level of the blood may be elevated for approximately one week following large doses of TEM.

THERAPEUTIC EFFECTS

Hodgkin's disease. All nine patients with Hodgkin's disease who were given TEM experienced definite subjective improvement within a few days. This

subjective improvement was manifested by a feeling of well-being, greater optimism, and increased appetite as soon as the transient nausea and anorexia abated. The duration of the subjective improvement was from a few days to three months.

Three patients who had not been treated with x-ray or HN2 previously had almost complete regression of peripheral lymph node enlargement. It is the authors' impression that the regression was somewhat slower than that observed following HN2. The diminution in size became apparent at three to seven days after completion of the course of TEM. With oral administration of TEM, regression usually commenced within a week. Although the data are insufficient for definite conclusions, it is the authors' impression that the remissions obtained in Hodgkin's disease with TEM were not as complete and did not last as long as those observed following treatment with HN2 in single doses of 0.3 to 0.5 mg. per kilogram of body weight.[2]

Two patients had previously received x-ray therapy but no nitrogen mustard. In both, remissions of one month were obtained with TEM.

Four patients had previously received both x-ray and HN2. Of these, two patients (Cases 2 and 5) were still responding to HN2, and also responded to courses of TEM with satisfactory remissions of two and one months, respectively. The remaining three patients (Cases 5, 6 and 9) did not respond to HN2 therapy, and also had no objective improvement following TEM. It is concluded that little or no benefit is to be anticipated in Hodgkin's disease from the use of TEM if HN2 is ineffective. Probably the obverse is true also: One patient continued to have undulating fever despite repeated courses of TEM, and was given a course of HN2. No dif-

Chart 3.—Clinical and hematologic course of a patient with Hodgkin's disease (Case 1) receiving TEM and HN2. There was no effect upon the undulating fever, although the enlarged cervical lymph nodes were considerably reduced in size and there was subjective improvement.

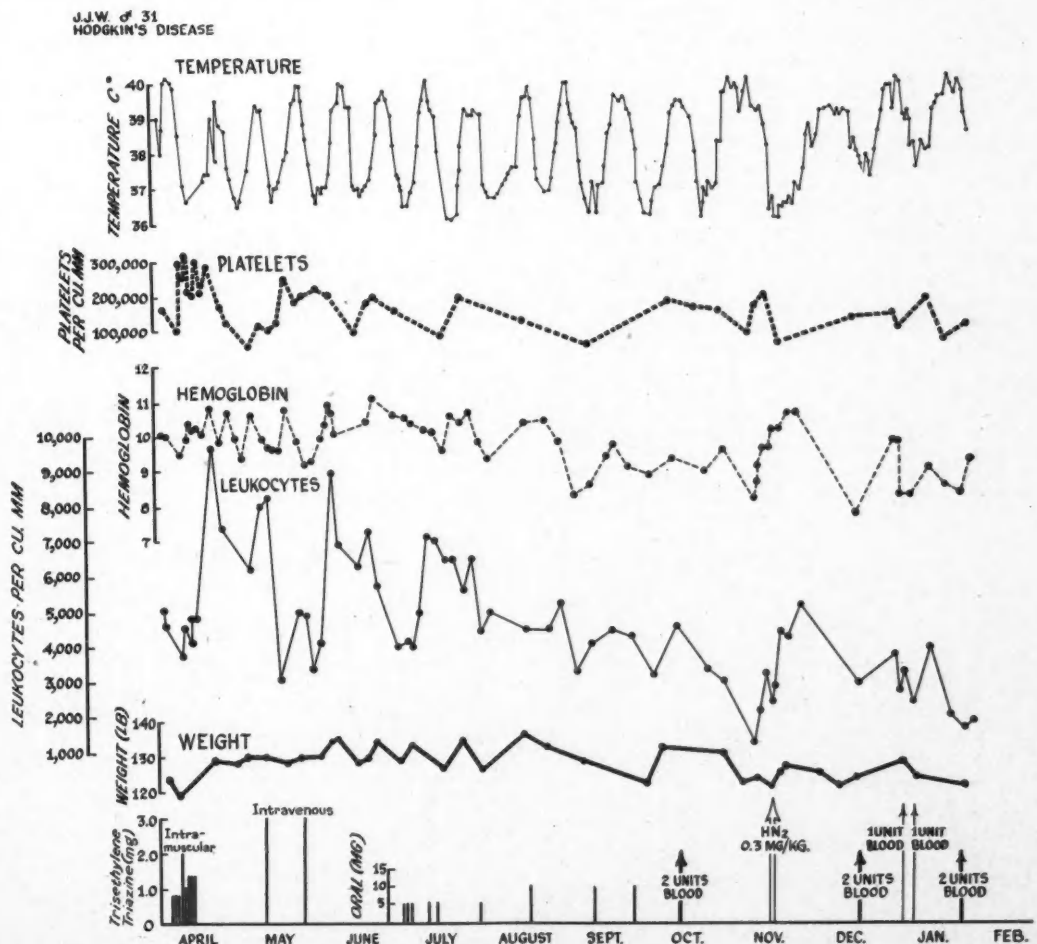


TABLE 1.—*TEM in the Treatment of Patients with Hodgkin's Disease and Other Lymphomas*

Case No.	Sex and Age	Duration of Disease (months)	Prior Therapy X-ray	Prior Therapy HN2	General Condition	TEM Therapy Route*	TEM Therapy Schedule† Admin./Days	TEM Therapy Total Dose (mg.)	TEM Therapy Dose (mg. per kg. of Body Weight)	Effect	Length of Remission (months)	Outcome Following Last TEM Therapy
HODGKIN'S DISEASE												
1.	M 31	54	—	—	Fair	IM	7/7	8.5	0.15	Good	1	
		55			Fair	IV	2/14	6	0.10	Good	1	
		57			Fair	O	9/90	60	.....	Fair	2	Living—4 months
2.	M 23	60	+	+	Fair	IV	1/1	10	0.16	Good	2	
		62			Good	IV	1/1	10	0.16	Good	1	Living—3 months
3.	F 23	10	—	—	Good	O	2/2	20	0.4	Good	1	
		13			Good	O	4/4	20	0.4	Good	2	
		14			Good	O	4/4	20	0.4	Good	2	
		15			Good	O	2/8	10	0.2	Good	1	Living—2 months
4.	M 68	12	—	—	Good	IV	5/5	16.5	0.26	Good	3	
		15			Good	O	3/3	15	0.25	Good	1	
		16			Good	O	4/4	20	0.33	Good	1	
		17			Good	O	7/14	55	0.9	Toxic	..	Living—5 months
5.	M 33	36	+	+	Fair	IV	2/8	9	0.15	Fair	1	
		37			Fair	O	1/1	10	0.16	None	..	
		37.5			Poor	IV	1/1	10	0.16	Poor	..	Died—1 month
6.	F 29	17	+	+	Poor	IV	3/3	6	0.13	Fair	0.5	
		17.5			Poor	O	1/1	10	0.22	None	..	Died—1 month
7.	M 28	12	+	—	Fair	IV	3/3	7.5	0.15	Good	1.0	
		13			Fair	IV	3/3	7.5	0.15	Fair	0.5	Died—2 months
8.	M 26	4	—	—	Fair	IV	3/3	8.1	0.15	Good	0.5	Living—1 month
9.	F 27	24	+	+	Poor	IM	3/3	5.6	0.15	None	..	Died—1 month
LYMPHOSARCOMA												
10.	M 39	5	—	—	Fair	IM	7/7	7.0	0.10	Good	2	
		5.5			Fair	IM	5/5	10.0	0.14	Good		
		7.5			Fair	O	2/2	10.0	0.14	Fair	0.5	Died—1 month
11.	M 32	25	+	+	Poor	IM	7/7	4.9	0.10	Fair	0.5	
		26			Poor	IM	4/4	6.4	0.12	Poor	..	Died—2 months
12.	M 55	6	—	—	Good	O	1/1	5	0.08	Good	1	
		8			Good	IV	2/3	2	0.03	Good	1	
		8.5			Good	O	1/1	5	0.08	Fair	0.5	
		9.5			Good	O	1/1	5	0.08	Fair	1	Living—1 month
LYMPHOCYTIC LEUKEMIA												
13.	F 67	48	—	—	Good	IM	3/3	3.5	0.05	Good	3	
		55			Good	IM	2/3	1.5	0.02	Good	2	
		57			Good	O	1/1	5.0	0.07	Fair	1+	Living—1 month
14.	F 5	4	—	—	Fair	IM	1/1	0.5	0.03	Fair	1	
		5			Fair	O	1/1	2.0	0.13	Fair	0.5	
		6			Poor	O	1/1	2.0	0.15	Poor	..	Died—1 month
MYELOCYTIC LEUKEMIA												
15.	M 38	18	—	—	Fair	IM	5/5	5.4	0.1	None	..	
		18			Fair	IV	2/2	2.8	0.05	None	..	Living—9 months
16.	F 63	140	+	—	Fair	O	2/4	10	0.13	None	..	
		142			Fair	O	5/30	30	0.4	None	..	Living—5 months
MYCOSIS FUNGOIDES												
17.	M 58	170	+	+	Poor	IM	5/5	14.0	0.24	None	..	Died—1.5 months
18.	M 70	24	+	+	Fair	IM	7/7	6.8	0.10	None	..	
		26			Fair	IM	7/7	10.0	0.24	None	..	Died—10 months

* IM—Intramuscular; IV—Intravenous; O—Oral.

† The figures indicate the number of doses and the span of time over which they were given. Example: 7/7 means seven doses in seven days.

ference in effect in controlling the disease was noted (Chart 3).

Objective evidence of improvement following TEM therapy was judged by the effect upon lymph nodes, spleen, fever, and pruritus. Lymph node enlargement was reduced considerably in four patients, and moderately in two. It was not affected in two patients in whom previous HN2 therapy had also been ineffective, and one patient had no palpable lymph nodes. Splenomegaly was present in two patients. In one, the spleen was reduced in size, becoming no longer palpable. In the other patient, no longer responding to HN2, no effect was observed. Five of nine patients (Cases 1, 2, 3, 7 and 8) gained weight, up to 5 kg., during the month following TEM treatment. The one patient in good condition who did not gain weight (Case 4) received excessive doses which resulted in anorexia and pronounced bone marrow depression.

Three patients (Cases 1, 2 and 5) had fever as part of the course of the disease. TEM had no effect upon the febrile course in two patients, but did produce a remission of one month in the febrile course of one patient. Three patients had pruritus. In two, the pruritus was controlled, with complete relief for approximately two weeks. In one patient (Case 5), no longer responding favorably to either x-ray or HN2, the pruritus was not affected.

Lymphosarcoma and lymphocytic leukemia. Three patients with lymphosarcoma were treated with TEM. One patient (Case 11) in poor condition had slight reduction in the size of cervical, abdominal and thoracic masses, lasting for about two weeks, with subjective improvement and a weight gain of 2 kg. One patient (Case 10) with a rapidly progressing lymphoblastoma, had good remission for two months following two parenteral courses of TEM. The third course, given orally, produced much less effect. The third patient (Case 12) had lymphosarcoma involving the cervical, axillary and inguinal lymph nodes. In this case the bone marrow cell count was 90 per cent lymphocytes. One oral administration of 5 mg. of TEM produced pronounced regression in lymph node enlargement and a decrease in the number of lymphocytes in the bone marrow to 20 per cent. Satisfactory improvement was achieved with a second intravenous course.

The hematologic course of one patient (Case 13) with chronic lymphocytic leukemia is recorded in Chart 4. There was a decrease in the number of leukocytes in the peripheral blood within a few days of therapy, followed by a slower reduction in cervical and axillary lymph node enlargement. The remission lasted for three months, and was again achieved by two subsequent courses of TEM.

Another patient (Case 14) had primitive cell leukemia, either lymphoblastic or monoblastic in type, with large submaxillary lymph nodes. Prompt decrease of the leukocyte count with disappearance of the immature cells occurred after one intramuscular administration of 0.5 mg. of TEM. The lymph nodes regressed to approximately two-thirds the original size during the next two weeks.

Other lymphomas. Two patients with myelocytic leukemia (Cases 15 and 16) were treated with TEM. No effects were observed on peripheral blood counts, on bone marrow, or on splenomegaly. There was no subjective improvement.

Two patients with generalized, advanced mycosis fungoides (Cases 17 and 18), who were no longer responding to the intravenous administration of HN2, were treated with TEM. Depression of the leukocyte and platelet counts, and temporary hypoplasia of the bone marrow were observed, without clinical improvement.

Other neoplastic diseases. As indicated in Table 2,

Chart 4.—Hematologic course of a patient with chronic lymphocytic leukemia (Case 13) treated with TEM. Associated with the decrease in the leukocyte count there was reduction in the size of cervical and axillary lymph nodes.

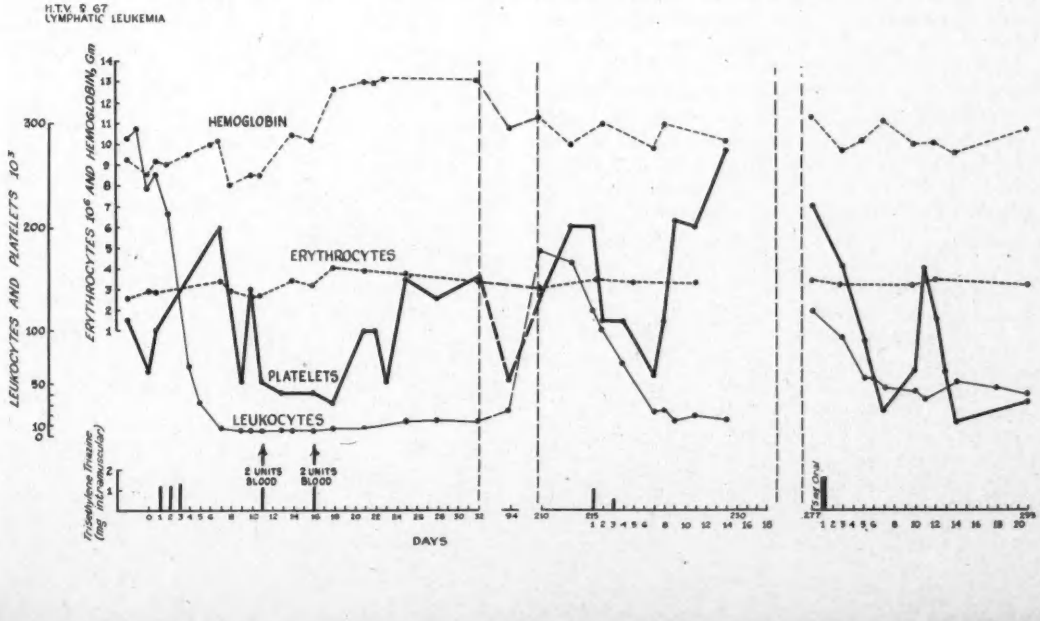


TABLE 2.—*TEM in Patients with Neoplastic Diseases Other than Lymphomas*

Case	Sex and Age	Diagnosis	Route*	Days Treated	Total Dose	Dose (mg./kg.)	Effect on Tumor
19.	M 54	Carcinoma nasopharynx	IV	3	28	0.5†	None
20.	M 71	Carcinoma nasopharynx	O	3	15	0.28	None
			O	1	15	0.28	None
21.	M 42	Carcinoma lung	IV	5	12.5	0.28	None
22.	M 36	Carcinoma lung	IA	1	10.0	0.21	None
23.	M 28	Carcinoma testis	IM	7	4.9	0.10	Minimal‡
			IM	2	1.4	0.03	None
24.	M 28	Carcinoma testis	IV	1	9.0	0.15	None
25.	F 51	Carcinoma breast	IM	7	6.5	0.10	None
26.	M 46	Carcinoma kidney	IV	1	10.0	0.14	None
27.	F 38	Melanoma	IM	3	14.0	0.25	None
28.	F 48	Melanoma	IV	1	11.0	0.20	None
29.	M 18	Osteogenic sarcoma	IA	1	15.0	0.25	None
30.	F 2	Wilms's tumor	IA	1	2.6	0.20	Minimal‡
31.	M 5	Neuroblastoma	IA	1	4.0	0.25	None
32.	M 26	Thymoma	IV	3	9.0	0.15	Minimal‡
			IV	2	6.0	0.1	

* IV—Intravenous; IM—Intramuscular; O—Oral; IA—Intra-arterial.
† This dose is fatal.
‡ Slight decrease in size of tumor masses for few days. All patients have died.

14 additional patients received treatment with TEM. No beneficial effects were observed. There was minimal but definite decrease in the size of the neoplastic mass in one patient with a teratocarcinoma of the testis, and in one child with a Wilms's tumor to whom TEM was administered through a catheter placed into the renal artery.[1] These effects lasted less than one week in each patient. In one patient with a thymoma which produced partial obstruction of the superior vena cava, treatment with TEM was followed by a reduction of the venous pressure from 28 to 12 cm. of water for approximately one week.

PATHOLOGY

Of the 32 patients in this series, nine of 18 patients with lymphomas, and all of 14 patients with other neoplasms have died. Necropsy was done in 21 of the 23 cases. The pathologic observations were similar to those in mice injected with TEM, and to those in patients following treatment with HN2.[12]

The changes in the tissues were dependent upon the dose of TEM administered and upon the time after the course of therapy. In general the cytotoxic effects were best noted in the bone marrow, the spleen, and to a lesser extent in lymph nodes.

No changes specific to the drug could be identified in the bone marrow earlier than one week following treatment with TEM. The most pronounced changes in the bone marrow were observed in cases in which autopsy was done between two and five weeks following the last course of therapy with TEM. The extent of the changes was in proportion to the dose of the agent. With doses of 0.25 to 0.5 mg. per kilogram of body weight there was complete disappearance of the cell elements. In the marrow the background was composed of remnants of supporting stroma, somewhat disrupted sinusoidal walls and small islands of an eosinophilic-staining, mucinous-appearing material, probably extravasated serum. Occasional pyknotic nuclei and primitive cells were observed in this completely aplastic marrow (Figure 1). Approximately seven weeks following therapy with doses of 0.25 mg. per kilogram of body weight the marrow was hypercellular. There were no changes in bone trabeculae, and there was no increase of connective tissue in the marrow.

In the spleen the changes followed a somewhat similar pattern, the lymphocytes being specifically involved. With doses of TEM above 0.25 mg. per kilogram of body weight, the earliest changes were

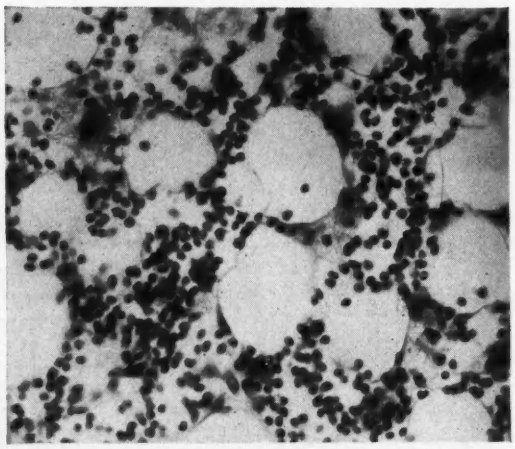


Figure 1.—Bone marrow of patient with epidermoid carcinoma of nasopharynx (Case 19), who died 11 days after receiving TEM, 0.5 mg. per kilogram of body weight, intravenously. Marrow elements are represented by a few large primitive cells in the stroma between fat cells; most of the remaining cells are erythrocytes. Hematoxylin- and eosin-stained. (X 320)

manifested by focal areas of necrotic tissue involving the tissue of a few Malpighian corpuscles (Figure 2). Within three weeks there was loss of lymphocytes from all of these areas, so that only the central arterioles remained. Considerable disruption of the red pulp, probably as part of the hemorrhagic diathesis, was also encountered. Later in the process the extravasated blood apparently degenerated and the pigment was contained within macrophages. Fibrous tissue proliferation occurred in the area of former lymphoid tissue. In other cases, in which smaller doses of TEM were given, no residual changes attributable to previous injury were observed in the spleen.

A few lymph nodes not replaced by tumor tissue were available for study. During the acute stages the lymphoid centers disappeared, the area consisting of the supporting stroma. Along with this there was considerable hyperplasia of the reticulum elements, many of these cells filling the sinusoids (Figure 3).

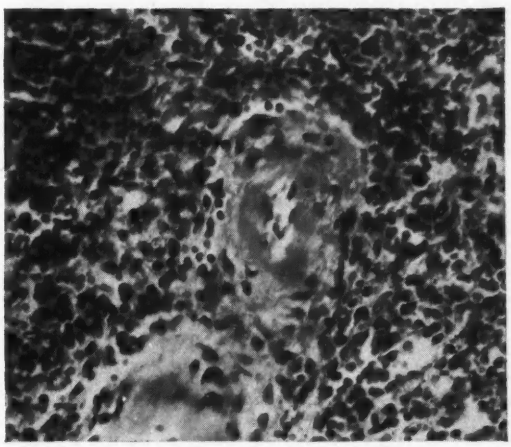


Figure 2.—Spleen of the patient in Case 19. Only a few lymphocytes remain of the lymphoid follicle and there is much extravasated blood in the pulp. Hematoxylin- and eosin-stained. (X 320)

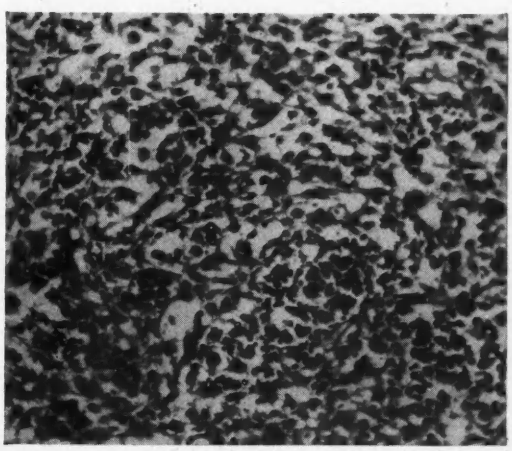


Figure 3.—Lymph node of patient with melanoma (Case 28) who died seven days following 0.2 mg. of TEM per kilogram of body weight, given intravenously. Lymphoid follicles are represented by a few groups of pyknotic lymphocytes and reticular cells form the bulk of the tissue. A group of melanoma cells appears in the lower center. Hematoxylin- and eosin-stained. (X 160)

An interesting change was observed in one patient with Hodgkin's disease (Case 6) who died during the stage of bone marrow regeneration. In the submucosa of the small bowel were masses of plasma cells in areas usually containing many lymphocytes. No specific changes were observed in the gastrointestinal tract in other cases.

In the patient who received TEM in a dose of 0.5 mg. per kilogram of body weight (Case 19), in addition to the extreme effects upon the bone marrow and the spleen there were hemorrhages into the pulmonary alveoli and on serosal surfaces and mucous membranes. There was complete arrest of spermatogenesis in the testes.

In many cases necrosis of the tumor was a prominent feature. However, since this is also observed at autopsy in untreated cases, it could not be ascribed specifically to the drug. No cellular changes could be identified, and focal areas of the type described by Spitz[12] in tumors of the lymphoma group following therapy with nitrogen mustard, were not observed.

DISCUSSION

The clinical results of the present investigation of TEM are in agreement with the results reported by other groups.[8, 13] Rhoads and co-workers[8] studied 15 patients with Hodgkin's disease treated with TEM given orally. Fourteen of them had improvement. Two patients who had pruritus were relieved, and high fever was controlled for up to six weeks in two additional patients. The usual duration of improvement was six to 12 weeks. Objective improvement was also observed in three of four patients with myelocytic leukemia and in three of six patients with lymphocytic leukemia, but two patients with lymphosarcoma did not respond. One patient with mycosis fungoides and one with plasma cell myeloma also did not improve.

TEM appears to be a drug of some clinical usefulness in the same conditions in which nitrogen mustard is of some value: Hodgkin's disease, lymphosarcoma, lymphatic leukemia and perhaps other lymphomas. The remissions of the disease are of short duration, and no evidence is available that the life span is prolonged. The pharmacologic and toxicologic effects of TEM are in general the same as those of nitrogen mustard. The advantages of TEM as compared with HN2 are as follows: (a) TEM can be given intramuscularly and orally as well as intravenously, thus obviating the occasional complication of phlebothrombosis produced by nitrogen mustard. The oral route of administration also allows more continual and more regularly spaced treatments than are perhaps possible with nitrogen mustard. (b) TEM produces much less nausea and vomiting than does nitrogen mustard. Headache and diarrhea are also reduced. Two patients of the present series refused any further therapy with HN2 because of

severe reactions of vomiting and headache, but were satisfactorily continued on TEM.

There are also definite disadvantages of TEM as compared with HN2: (a) TEM has a narrower chemotherapeutic range than nitrogen mustard. With TEM given parenterally, 0.5 mg. per kilogram of body weight is fatal, and a single course should not exceed 0.25 mg. per kilogram of body weight. With oral administration, 0.4 mg. per kilogram of body weight, given in daily doses of 5 to 10 mg., appears to be the upper level of safe dosage for a single course of approximately one week. (b) Lymphocytic leukemia appears to be extremely sensitive to TEM. The first course, given intravenously or intramuscularly, should not exceed 0.05 mg. per kilogram of body weight, and oral dosage should not exceed 0.1 mg. per kilogram of body weight. This caution is applicable not only to lymphocytic leukemia with frank leukemic blood picture but also to subleukemic lymphocytic leukemia and to lymphosarcoma with bone marrow involvement. (c) The ease of administration of TEM, particularly orally, and the minimal immediate reactions are hazards as well as advantages. The severe effects on the bone marrow and the narrow chemotherapeutic range make imperative the closest clinical and hematological observation for at least three weeks following the termination of the therapy.

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Attitudes Toward the Dubious Compensation Claim

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SUMMARY

Laws providing for compensation of workmen for occupational injury are a powerful socio-economic force.

In settlement of compensation claims the goal, difficult to achieve, is fairness to employee, employer and insurance carrier. Often, medical, legal, economic and social considerations conflict with one another. A "fact" in one field may not be considered so in another.

Since medical data and testimony often guide the ultimate decision of a compensation claim, the physician's attitude is a large factor not only immediately and directly in determination of the case at hand but, perhaps more important, in the ultimate direction of the socio-economic forces which spring from the sum of all such determinations.

To perpetuate the good in workmen's compensation laws, the next generation of physicians—and of lawyers and business administrators as well, for they, too, are involved—ought to have basic training in the social sciences in order that they may have a broad rather than a segmental view of the problems with which they deal.

WORKMEN'S compensation laws have, in four decades, resulted in initiating powerful forces which have altered and are continuing to alter the economic status, the sociological relationships, and the systems of belief of the entire employed population, all employers, all insurance carriers, and large segments of the medical and nursing professions. It is probable that the magnitude of these changes has not yet been fully realized, and that most of the forces contributing to the total changes have not yet reached their ultimate effect.

It may be a generation before the social scientists will present a truly complete and objective account of the interacting forces which are profoundly affecting the total employed population in the United States. The object of this presentation is to offer some tentative opinions which may be of assistance in orienting physicians in this still changing pattern of social forces.

One of the first states to have such laws, California passed its first Workmen's Compensation Insurance Act in 1911. In its present form, under the extensive revision in 1917 of a more comprehensive act adopted in 1913, it is one of the most liberal laws in the 48 states, allowing unlimited medical care, provides relatively high compensation indemnity, includes coverage of "aggravation of a pre-existing condition," and resolves doubt in favor of claimants. The word "injury" applies to any occupational disease. These liberal factors are generally accepted as being positive values and worthy of perpetuation.

This presentation will point out some trends which are believed by many observers to be inimical to the best long-term interests of the act and its beneficiaries, as well as to the medical profession, and will offer some explanations as to the origin of those trends. The words "liberal" and "liberalization," which have no fixed value, will be used frequently, and the reader must assess the values to be attached to the words according to their application in the text.

One has but to be familiar with the compensation laws of some other of our 48 states to recognize that California has indeed a liberal compensation act. Some states, for instance, limit the total cost of medical care to some sum such as $500, an amount which can be used very readily in two or three days of hospitalization for serious injury. Californians may be justly and properly proud of this liberal act. There is no intent here to criticize the California Workmen's Compensation Act or to appeal for a return to the "good old days." The good old days before the compensation laws existed were most certainly not so good for the injured employee. How bad they were is beyond the memory of the present younger generation. Industrially injured employees did not have even a remotely fair opportunity of being restored to health or of being supplied with sustenance without a court fight in which both the common law defenses and the court procedure were hurdles which they could seldom overcome.

Legal and claims authorities state that the act is administered under a philosophy described as "liberal interpretation of the law." The liberality of the act and the liberality of its interpretation are clearly and interestingly documented by Thomas,[1] chief counsel of the State Industrial Accident Commission, San Francisco, who noted that it "became the social policy of California to provide a means whereby substantial justice could be accomplished in all cases expeditiously, inexpensively, and without encumbrance. As part of that policy, it is provided by law that the benefit of any doubt must be given to the injured employee."

Most Americans, be they physicians or laymen, understand that fellow citizens in an unfortunate situation are customarily given the "benefit of any reasonable doubt." When it becomes more generally understood that under the compensation act—

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as currently interpreted, at least, by the Industrial Accident Commission's counsel—the claimant must be given the benefit of "any doubt," a partial explanation will be supplied for awards in favor of applicants whose claims appear rather dubious.

A more complete explanation of awards which sometimes puzzle physicians lies in the statement made frequently by compensation authorities but difficult to find in print—in medical literature, at least — that the compensation law is administered not only with "liberal interpretation of the law," but also with "liberal interpretation of fact." Thomas illuminated this point in a continuation of the paragraph already quoted: "Likewise, since the applicant in proceedings before the Commission is frequently an injured employee acting on his own behalf without legal aid, the rules of evidence were relaxed for his benefit. Therefore, in proceedings before the Commission the technical rules of evidence, particularly the hearsay rule, are not enforced, and rather wide latitude is permitted. The injured employee cannot be expected to procure medical reports from experts or specialists, but generally must rely upon reports of his family doctor or an attending physician who may not have the facilities for preparing an elaborate report. Consequently, injured employees are given benefits and considerations which are not accorded plaintiffs in the civil courts."

Illustration may help toward understanding that paragraph. Most physicians who have treated any appreciable number of industrial injuries are familiar with cases in which disease, not necessarily nor even usually caused by trauma, is demonstrated and disability exists—and yet there has been nothing in the history to account for any causal relationship between the employment and the disease. Moreover, there may have been repeated denials to the attending physician and to consultants, and to representatives of claims departments, of any accident, incident or event — and these denials may have been repeated many times over a period of many months. The award, when finally granted after a hearing before the Industrial Accident Commission, is based on the "fact" that the claimant at his hearing recalled a specific incident on a specific date at a specific time—not one detail of which had been recalled previously, but on the contrary had been denied many times previous to the hearing. This is a simple example of the "liberal interpretation of fact."

The same "liberal interpretation of fact" is applied to symptoms. A claimant with an apparently healed fracture in perfect alignment, causing no demonstrable disability of any kind, and described as "well" in the final clinical note, may be granted an award on the basis of a statement of pain or of some other complaint which cannot be verified.

Most California readers are familiar with the "aggravation of preexisting condition" clause, and it is not necessary for their benefit to elaborate on the statement that this clause is being interpreted much more liberally than in the 1930's.

To illustrate the increased liberality in the administration, Thompson[2] discussed myocardial infarction. Referring to liberalization by statute he stated, "The so-called Presumptive Act of the State of California is such that heart disease or pneumonia developing in any fireman or policeman is accepted as an industrial illness unless unequivocably proved otherwise." Also pertinent is Thompson's statement: "It has been pointed out that from the standpoint of industrial medicine the acceptance or the non-acceptance of the industrial origin of an injury or an illness is determined by the legal profession and public opinion, as this is carried out by the administration at state and possibly national levels. The gradual inclusion of more and more clinical conditions as industrial injuries is well known to all of us and the example of myocardial infarction is used to illustrate the progress being made toward this end."

This underscores the pressure on the practicing physician of today to ignore the application of scientific knowledge of etiology, and instead of offering a sound medical opinion which he should be qualified to express, to substitute an unsound legal opinion which attempts to anticipate the currently fashionable decisions of the Industrial Accident Commission. These are indeed unstable criteria on which to base a diagnosis. If the physician chooses to continue to express a medical opinion based on sound medicine, he risks being publicly overruled as being antagonistic to the patient's welfare and out of harmony with the philosophy of the administrative body to which the report will be presented — and appearing to have caused treatment to be delayed until after the hearing. If he attempts to compromise between sound medicine and fashionable decisions, he will undergo a frustrating experience.

It is because of these situations that the physician appears to have a most legitimate interest in the philosophies of compensation claims administration. Medical principles dictate a scientific approach to the facts, and these facts if well established medically may not be distorted or altered because of expediency. This is of vital importance to the physician, and is of vital importance to the practice of medicine. More on this later.

If it be stipulated that a liberal compensation law is being administered with liberal interpretation of the law and liberal interpretation of fact, is there a reasonable explanation as to why this compounding of liberalization has come about?

A most plausible explanation is at hand when one considers that there are three classes of unemployed persons for whom relief by law has been made available. These three classes are:

1. Those who are unemployed because of industrial injury.

2. Those who are well but for whom employment is not available.

3. Those who are unemployed because of non-industrial disability.

Relief by law in California has been supplied for all three classes in the order in which they have been listed above. The Workmen's Compensation Law for the relief of industrial injuries was passed originally in 1911 (financed at employer's cost); relief for the unemployed through the State Unemployment Insurance Act was enacted in 1938 (at present financed at employer's cost); and the Unemployment Disability Insurance for persons with non-industrial disability became effective in 1946 (at employee expense unless the employer elects to contribute).

For 35 years — from 1911 to 1946 — a disabled claimant appearing before the Industrial Accident Commission was either granted an industrial award, or he was left dependent on his own resources, in the lack of which he became indigent. This constituted such a powerful appeal to administrators that it was difficult to feel that any great over-all social injustice was done if considerable latitude and liberality were exercised in classifying many extremely dubious claims as being industrial.

In other words, liberality of interpretation both of the law and of the fact appear to have sprung up for very natural reasons and as an inevitable reaction to fill the vacuum created by need. Insofar as the vacuum is now at least partly filled by the current Unemployment Insurance and Unemployment Disability Acts, the social justification for overliberalization (if such has existed) should be in diminuendo. Some social pressure for liberality may still exist if decisions are influenced because the benefits of the Compensation Act are considerably greater than those of the Unemployment Disability Act and because it is employer rather than employee funds which are to be expended under the compensation award.

If it be granted that these rather superficial, oversimplified observations are correct, one may legitimately ask why they concern physicians.

One very profound effect of the introduction of the compensation law has been to alter the doctor-patient relationship by the introduction of the third party. In compensation cases, this third party is the employer, to whom is usually added the fourth party —the insurance carrier; and in the disputed claim there is the fifth party, the Industrial Accident Commission.

Patients with industrial injuries seem, on the basis of their attitudes, to be of three classifications:

A. Those whose ability to work is viewed realistically in terms of the actual physical disability, job requirements, and the therapeutic needs. (This is the normal, healthy attitude.)

B. Those whose emotional attitudes cause resistance to work, which the actual physical disability does not justify. (This is unhealthy and is generally recognizable, at least when it exists in considerable degree.)

C. Those whose emotional drives to work are so strong that their insistence on working is unrealistic in terms of actual disability, of job requirements, or of therapeutic needs. (This may be more frequent than is recognized and, at least in its extreme, may —like attitude "B"—be unhealthy.)

Also, parenthetically, it should be remarked that a patient does not necessarily stay in the same class during the entire length of the claim. Occasionally, the intrinsic mental dynamics of the patient will undergo a change. At other times either skill or awkwardness in the physician's handling of the patient or in the layman's processing of the claim will alter the attitude. This is important as a reminder that efforts should be directed to maintain the healthy attitude of the one class, and to alter beneficially the attitude of the other two.

Ordinarily, the compensation cases of patients in Class "A" do not constitute a major problem in medical or claims administration. Neither do patients in Class "C" usually find it necessary to become involved in any type of dispute to obtain their rights. In Class "B" fall the majority of cases which cause the greatest difficulty in the diagnostic, the therapeutic and the claims field. When awards based on expediency are granted, the beneficiary is most likely to be one of this group.

A full discussion of all the possible dynamics which cause patients to fall into Class "B" is not within the scope of this presentation. It might be mentioned, however, that in this class may be found those who carry hostilities or anxieties of any kind, or are insecure from any cause. The dependency on a compensation award may lie in a work situation to which the claimant is poorly adjusted and from which he wishes to escape, or it may be a reflection of a basic inadequacy totally unrelated to any work situation. Occasionally, one can clearly discern the effect of what Freud describes as "the advantage of an illness," but since the economic, the social, and the psychic maladjustments may be so interwoven, skilled psychiatry may be required to accurately uncover the mental dynamics causing the dependency. It is the author's belief that a well integrated person is seldom found in Class "B," and, if found, that he will seldom remain in that category for long. Also, it is probable that patients can be removed from Class "B" and promoted to the healthier Class "A" in direct ratio to the psychiatric or psychosomatic interest and skill of the attending physician. Laymen also—be they supervisors, employers, claim agents, business agents or any others involved in the handling of the claim or in contact with the claimant—may materially affect the claimant's emotions to his benefit or detriment.

As a subject for practical research for both physicians and social scientists, the thorough and complete study of Class "B" should offer an interesting challenge. The social scientists involved in such a thorough study should include those versed in the practical aspects of the disciplines of economics, psychology, sociology and cultural anthropology to supply all the contributions necessary to analyze the environmental pressures causing the psychic or psychosomatic phenomena.

Granted that such a study, if thorough, would be an ambitious long-term project, its contribution to justice in determining claims should be tremendous. Of course, with varying degrees of success, there are efforts now to present a complete picture of individual cases, but the Commission is still too frequently compelled to depend upon the use of intuition in rendering a decision. Although it seems improbable that all the sciences collectively will ever abolish the need for intuition in forming a judgment, the necessity for its use in considering claims may be greatly minimized if the potentialities of a cooperative study by the social sciences are ever realized.

The well recognized so-called "arbitrary award," very closely related to or synonymous with the intuitive award, perpetuates itself and multiplies by inviting more claims which result in more awards of a similar character—and there is now a well-planted common belief that any claimant who has been injured is "entitled to something" over and above medical care and compensation for the period of temporary disability.

To return to the subject of "liberalization of fact," the author believes that medical statements as to cause and effect (the etiology of the pathologic condition) must be based on medical facts and medical principles, and that these facts may not be stretched or altered because of expediency. The house of medicine will collapse entirely if the study of causes—one of its cornerstones—is to be subject to personal or social expediency. When the weight of medical authority states that beyond a reasonable doubt a given clinical syndrome is "X" disease, it would seem only reasonable that this and all identical cases should be invariable classed as "X" disease. When the administrative authorities of the state find it mandatory by statute, or expedient through interpretation of the law or through interpretation of fact, to render a decision which cannot be overruled by any court that a claimant who has what is described medically as "X" disease really has "Y" injury instead, a chain reaction is begun which will have serious long-term effects on the practice of medicine—and this event should cause concern.

It is not to be denied that individual physicians have contributed to these decisions which physicians collectively deplore. The Industrial Accident Commission must have some justification for its decisions and usually, if not always, there is a report from some physician which either intimates or states that "X" condition might be "Y" injury. It is not unusual to see a two-page medical report describing "X" condition ending with one sentence saying in effect, "Of course 'Y' injury is possible." Frequently the medical examiner is unconsciously ambiguous and he is unaware that a single sentence has nullified the intent of his entire report. In other cases, however, he may deliberately — due to an understandable sympathy for the patient—go out of his way to assist the patient to the extent of indicating an impossible medical situation. This contributes most materially to making it possible to reach a legal finding that asserts what may well be a medical impossibility. The medical profession must not adopt too self-righteous an attitude toward those who sacrifice principle to expediency, because physicians are not unanimously immune to this powerful influence.

It has frequently been advocated that a medical board be established within the Commission to evaluate the medical aspects of all claims. This procedure is established in some other states, and its proponents claim it has practical value as well as theoretical merit.

Those who profit by awards through expediency should not, in the long term, suffer loss if the tide is reversed and principles become paramount over expediency. Expediency which wins benefits through social pressure can ultimately work against present beneficiaries when the pressure of expediency becomes great enough from another quarter. It would seem fair to state that long-term, consistently fair, uniform distribution of benefits will be assured only if all concerned—administrator, physician and beneficiary — understand the fundamental principles involved, honor them, and respect the procedures established and based upon them. The tenure of the personnel on today's scene is limited, at the longest, to a lifetime. Viewed over this relatively short span, the long-term effects of expediency versus principle may not seem serious. Respect for the long-term true interest of whatever administrative, professional, or labor group to which any of those concerned owes allegiance, seems to dictate a conscientious recognition and honoring of sound principles.

The attitudes of the injured, the Commission, and the physician have been discussed in some detail. That the other groups equally involved in claims settlements — the employer, the insurance carrier, and the labor union — have been mentioned only casually does not mean that they are detached from the situation. In their own areas they are subject to similar conflicting pressures of expediency versus principle.

In any situation involving conflicts of beliefs and attitudes between groups, the social "law of the vicious cycle" operates, and either regression or improvement in the attitudes of any of the parties concerned will influence the position of all other interests. Since the Industrial Accident Commission, the clearing house for all claims, is in a position of greatest leverage to change attitudes toward dubious claims, its part in the total situation has been stressed.

There is question whether the dominance of expediency over principle, insofar as it be evident in the compensation insurance field, is a problem primarily of this one field. It seems proper to suggest that the phenomenon is merely a reflection of a nationwide pattern extant in all areas of American life.

The first social security program of the compensation insurance type was introduced in Germany at the time of Bismarck, and it was 60 years before its costs showed any appearance of beginning to level. The costs in California have risen very much

more rapidly in much less time, and the upward trend seems to be proceeding with little diminution of speed.

Social scientists, in personal discussion, have pointed out that the Germans—at least during the period referred to—had a rather universal respect for authority, both individual and institutional. The modern American attitude, on the other hand, was contrasted as being increasingly, for at least 40 years, in conflict with authority (or restrictions by authority) of any type—whether it be personal or institutional, governmental or corporate, temporal or religious. The old-time principles of personal integrity have been giving way to the motto "It's all right if you can get away with it" on all levels of American life in too many areas of social existence.

At the same time there has developed, at the administrative level, a generally enlightened attitude toward socio-economic obligations. This has resulted in accelerated programs of supplying, directly or indirectly, financial assistance for many groups previously neglected. These programs have, in one generation, resulted in an entirely new concept by administrators—be they at national, state or county levels—toward the distribution of expendable funds, whether they be public or corporate. The continuation of such enlightened programs must inevitably depend upon public support. Factors which weaken public support may be economic, social and political. In the administration of all such programs, it should be borne in mind that public resistance, always present in some degree, may swell to great proportions if sparks of economically or socially justified criticism be fanned by strong winds of political prejudice. The "all or nothing" principle then would apply, with partisans divided into "all for it" or "all ag'in' it" groups. A careful approach to the whole problem on a deeper basis, with study of each individual facet of the total situation, should be of great service in insuring perpetuation of the positive values in a soundly liberal Workmen's Compensation Insurance Act.

Most administrators, physicians and lawyers have not been sufficiently trained in the basic fundamentals of the social sciences to adequately understand and anticipate—let alone alter—social forces of the magnitude, and with the momentum, of those set in motion by workmen's compensation laws.

The present generation has two courses open. The first is for each to confine his efforts to his purely professional role, permitting the ultimate pattern of compensation to take shape as it will. The second course is for us, to the extent of our ability, to orient ourselves in the basic principles of economy, clinical psychology, sociology and cultural anthropology, and be better—if not thoroughly—prepared to influence the trends in compensation insurance. We will have valuable assistance in this if we step out of our ivory towers of practical experience, knock on the doors of the halls of learning and invite the interest of those who have the academic knowledge of these disciplines, but who now, too frequently, are isolated behind the ivy-covered walls.

And to the practitioners of professions in the next generation we should offer a better choice than either to ignore the social implications of their life work or to awkwardly grasp for belated help. We ought to insist that our educational institutions make basic courses in the social sciences mandatory for students of business administration and for the premedical and prelegal students. If this is done, the next generation may—with greater facility—improve and perpetuate present means of financial aid, medical care and rehabilitation for the injured workman.

California and Hawaiian Sugar Refining Corporation.

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CASE REPORTS

- Pheochromocytoma
- Dermoid Cyst of the Omentum
- Bronchiogenic Cysts
- Circumcaval Ureter

Pheochromocytoma

Report of a Case with Preoperative Diagnosis and Removal Through Anterior Abdominal Incision

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WITH the introduction of the "benzodioxane test" by Goldenberg, Snyder and Aranow[4] in 1947 and the "histamine test" by Roth and Kvale,[5] a means was provided of diagnosing the presence of epinephrine-producing tumors (pheochromocytomata) with a fair degree of accuracy, even in patients with persistent hypertension from the long continued effect of the secretion of such a tumor.

In a majority of reported cases, successful surgical removal of all pheochromocytoma tissue has produced a lasting restoration of blood pressure to normal. The following case is presented to illustrate a typical example of a pheochromocytoma diagnosed by the use of benzodioxane (933F or 2 piperidine - methyl - 1,4 benzodioxane) and histamine tests and removed successfully by way of a transverse anterior abdominal incision.

The patient, a 36-year-old white poultryman, was referred to Wadsworth General Hospital on May 10, 1949, because of hypertension. Blurred vision in the left eye had developed approximately six weeks prior to admission and blurred vision in the right eye three days before admission. Since 1943 the patient had had frequent headaches, described as throbbing in nature. Often during a severe episode of headache he would have a sensation of seeing blinding light, which was synchronous with each heartbeat. Frequently the headaches were accompanied by "cold sweats" and a sensation of trembling and shakiness.

The patient also noticed the gradual onset of dyspnea on exertion during the six months prior to admission. He had nocturia (two to three times) and, on one occasion, three months before admission, the urine was pink in appearance. There had been a weight loss of ten pounds during the previous six months.

PHYSICAL EXAMINATION

Upon physical examination the patient was observed to be well developed, moderately well nourished, and apparently not in acute distress. The temperature was 98.6° F., the pulse rate 110, and respirations 16 per minute.

The pupils of the eyes were round and equal and reacted to light and accommodation. Extraocular movements were normal. Papilledema was present in both eyes—one diopter in the right and two in the left. There was generalized and localized attenuation of arterioles and a two and one-half to one vein-artery ratio. There was mild arteriovenous compression and copper-wire appearance of the arterioles. Flame-shaped hemorrhages and cotton-wool exudates were observed throughout the fundi of both eyes. Visual acuity was 20/40 in each eye.

The heart rate was rapid and was in normal sinus rhythm. There was no cardiac enlargement to percussion. A coarse grade II systolic murmur at the apex was noted. The blood pressure was 160 mm. of mercury systolic and 120 mm. diastolic.

The liver was palpated about one fingerbreadth below the costal margin.

LABORATORY EXAMINATIONS

Results of laboratory examinations of the blood were reported as follows:

Erythrocytes	4,100,000
Hemoglobin value	82 per cent
Leukocytes	11,000
Neutrophils	65
Lymphocytes	31
Monocytes	1
Eosinophils	1
Basophils	2
Sedimentation rate	20 mm. in one hour
Urea nitrogen	34 mg. per 100 cc.
Sodium	141 milliequivalents
Potassium	4.5 milliequivalents
Chloride	100 milliequivalents
Urea clearance	31 per cent
Serologic tests	Negative for syphilis

Specific gravity of the urine in a Fishberg concentration test was 1.016, 1.020 and 1.016. There were 100,000 hyaline casts, 100,000 granular casts, 4,500,000 leukocytes, 3,100,000 erythrocytes, and 500,000 epithelial cells in a concentrated urine specimen (Addis method). In routine urinalysis, five to eight leukocytes per high power field, and a few fine and coarse granular casts, were noted. The reaction for albumin was three plus. Urinary protein excretion (Esbach method) was 0.84 gm. in 24 hours. In an electrocardiogram there was a small Q in V_1, flat T in AVF, low T_1 and T_2, flat T_3 and a small Q in V_4, V_5 and V_6. The tracing was interpreted as being abnormal but not diagnostic. An x-ray film of the chest was normal.

In an intravenous pyelogram (Figure 1) the right kidney was observed to be essentially normal. The left kidney was poorly visualized but no definite mass could be seen. Carmelin blue dye injected intravenously was excreted poorly by both kidneys.

BLOOD PRESSURE STUDIES

Pronounced variations were noted in daily blood pressure determinations. The range was from 152 mm. of mercury systolic and 92 mm. diastolic to 260 mm. and 160 mm. respectively. At the time the highest level was recorded, the patient complained of severe, throbbing headache. This

Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

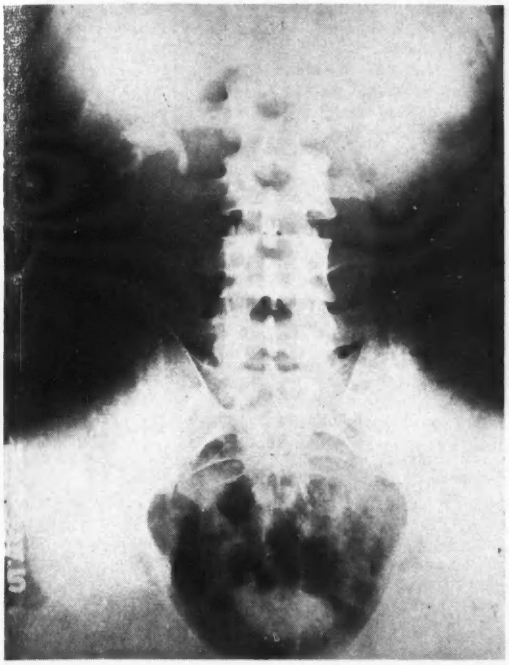


Figure 1.—Intravenous pyelogram showing inadequate visualization of the left kidney. This was thought to be due to the presence of a pheochromocytoma on the left. However, intravenous pyelogram following operation was similar to preoperative film.

episode was accompanied by coldness of skin associated with cold perspiration covering the body, a "glassy-eyed" appearance, and a slightly dazed condition. These symptoms subsided after about an hour, at which time the blood pressure was 160 mm. of mercury systolic and 120 mm. diastolic. The patient stated that he had had numerous similar episodes. A benzodioxane test was done May 23, 1949. Twenty milligrams of benzodioxane was given intravenously. The blood pressure decreased from 174 mm. systolic and 124 mm. diastolic to 150 mm. and 78 mm. respectively within four minutes (Chart 1). Seven minutes later the blood pressure was 160 mm. systolic and 100 mm. diastolic. The test result was considered positive. On May 26, 1949, a Roth-Kvale test was carried out. The blood pressure at the time of intravenous injection of 0.025 mg. of histamine was 150 mm. of mercury systolic and 100 mm. diastolic. Five minutes later it was 240 mm. and 170 mm. respectively. At this time, the patient complained of headache; the skin was cold and clammy, and there was cold perspiration over the entire body. An ampule of benzodioxane was opened, but the drug was not given because the blood pressure began to decline. (See Chart 2.)

Upon massage of the abdomen in the region of the left adrenal gland the blood pressure rose from 142 mm. of mercury systolic and 92 mm. diastolic to 150 mm. and 94 mm. respectively. With massage of the corresponding position on the right side, the pressure rose from 140 mm. systolic and 96 mm. diastolic to 144 mm. and 100 mm. The changes in pressure were not considered significant. On May 31, 1949, three weeks after the patient was admitted to the hospital, bilateral exploration of the adrenal glands was carried out. The preoperative diagnosis was pheochromocytoma of the left adrenal cortex.

Chart 1.—20 mg. benzodioxane produced a pronounced fall in the blood pressure. Curve is consistent with diagnosis of pheochromocytoma.

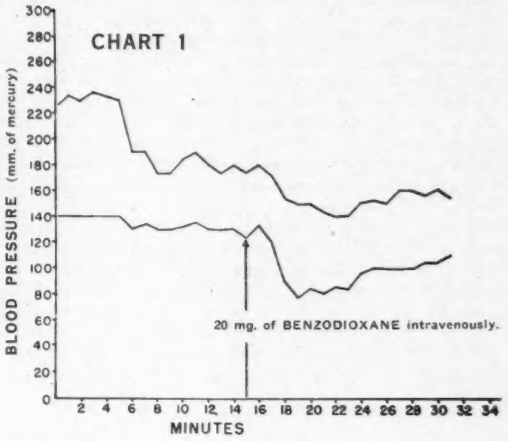
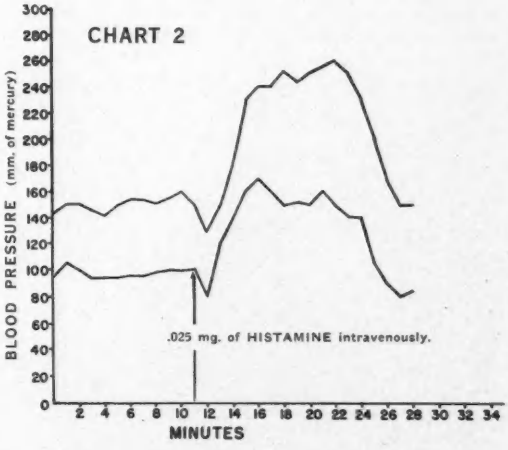


Chart 2.—Record of blood pressure following injection of 0.025 mg. of histamine, showing typical rise associated with pheochromocytoma.



OPERATION

The patient was anesthetized with cyclopropane and ether and the peritoneal cavity entered through a long, bilateral, subcostal, curved incision. The region of the right kidney and right adrenal gland was palpated; the right kidney was in normal position and of normal size. The right adrenal gland could not itself be identified, but there was no evidence of tumor in this area. In the region of the left kidney a mass, 7 to 8 cm. in diameter, was palpated. It lay along the upper pole of the left kidney, in the retroperitoneal space. The stomach was retracted downward and the lesser omentum incised in a direction parallel to the lesser curvature of the stomach. The left gastric vessels were rather long and it was possible to retract these to the right with a Deaver retractor. The lesser omental bursa and the tumor were exposed upon retraction of the lesser curvature of the stomach to the left. The peritoneum over the tumor was incised. The splenic vein and artery were identified and the pancreas, together with these vessels, was retracted downward, a procedure which exposed the anterior surface of the tumor. A large adrenal vein, about 7 to 8 mm. in diameter, coursed

along the lower anterior border of the tumor and entered the left renal vein. The anterior approach permitted excellent exposure of this vessel for ligation and division. During the period of manipulation of the tumor, the patient's systolic blood pressure rose to 220 mm. of mercury. This pressure was not affected by ligation of the large adrenal vein. The tumor was completely encapsulated and was readily mobilized by blunt dissection. Doubly clamping, dividing and ligating the overlying tissue and vessels freed all except the posterior-inferior surface of the tumor. The splenic flexure of the colon was mobilized and retracted medially. Geronta's fascia was opened and the tumor was approached from the lateral inferior surface. This area was mobilized without difficulty, and the tumor was delivered into the peritoneal cavity. The remaining pedicle of the tumor was divided and ligated. At this time there was pronounced decrease in the blood pressure, but at no time did the systolic pressure fall below 100 mm. of mercury. The lateral opening in Geronta's fascia was closed. The abdominal incision was then closed in layers with catgut and silk. The patient withstood the operative procedure well and his condition remained good throughout.

DESCRIPTION OF SURGICAL SPECIMEN

The specimen consisted of a rather flat, ovoid, encapsulated, brownish tumor mass, approximately 8 x 6 cm. in greatest dimensions and up to 3 cm. in thickness. The capsule had apparently been slightly torn in one area in the course of surgical removal. Remnants of yellow attenuated adrenal cortex extended over a portion of the surface, covering an area about 5 cm. in length. The sectioned surface of the tumor was dull brown and was studded here and there by pinpoint hemorrhagic flecks.

In microscopic examination of numerous sections, a rather uniform cytologic pattern composed of large, polyhedral or spindle-shaped chromaffin cells was noted. The chromaffin cells contained abundant, finely granular cytoplasm which stained a peculiar dark magenta with hematoxylin and eosin. The tumor tissue was permeated by smaller and larger congested blood channels and it was mainly about these vessels that the whorls and bundles of tumor cells appeared to be oriented.

In one of the sections, residual adrenal tissue upon the surface of the tumor was observed. This tissue was composed largely of cortex, but did contain a compressed central strip of medullary tissue, the cells of which resembled those of the neoplasm.

The pathological diagnosis was pheochromocytoma of the adrenal medulla.

POSTOPERATIVE STUDIES

The patient received five milligrams of desoxycorticosterone acetate the day before operation. During the operative procedure, he received 1,000 cc. of blood intravenously and 10 cc. of Eschatin® intravenously immediately following the removal of the tumor. Epinephrine in oil was administered on six occasions during the first two postoperative days. The patient also received 10 to 20 cc. of Eschatin daily for one week postoperatively.

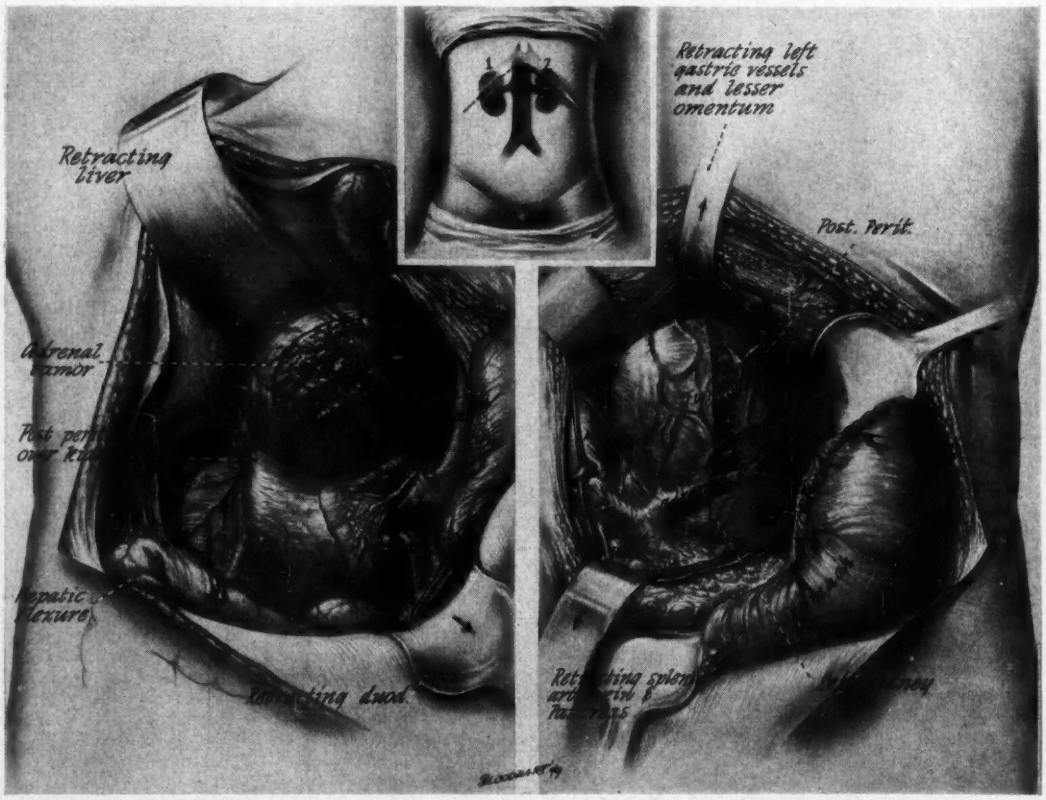
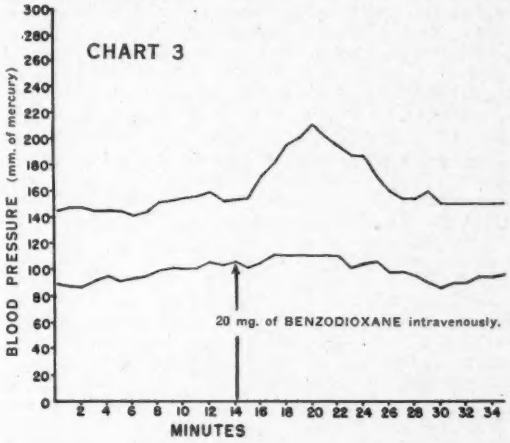


Figure 2.—Exposure of adrenal area through subcostal incision. *Left*—subcostal incision used in case reported, indicating exposure of tumor. *Right*—artist's conception of similar tumor of right adrenal gland exposed through right subcostal incision.

Following the patient's recovery from the operation, the blood pressure continued to be somewhat elevated, ranging from 140 mm. of mercury systolic and 80 mm. diastolic to 160 mm. and 100 mm. respectively. Urea clearance, determined June 20, 1949, was 72.5 per cent. Urea nitrogen in the blood was 14 mg. per 100 cc. A benzodioxane test was performed June 25, 1949. The blood pressure was 150 mm. of mercury systolic and 100 mm. diastolic before benzodioxane was given. After intravenous injection of 20 mg. of benzodioxane the blood pressure rose to 210 mm. systolic and 110 mm. diastolic and then gradually returned to 142 mm. and 90 mm. over a period of 15 minutes (see Chart 3). This was considered to be a rather typical response of essential hypertension. In an examination of the eyes on August 16, 1949, pronounced improvement was noted. There was no papilledema present. Although minimal constriction of some of the veins at arteriovenous crossings was observed, there was no deflection of the veins. There was some residual evidence of absorbing hemorrhage in both eyes. Cotton-wool exudates were not present. There were only minimal sclerotic changes in the retinal arterioles. Visual acuity in the right eye was 20/30, and in the left eye 20/30. An electrocardiogram was normal. Specific gravity of the urine (Fishberg concentration test) on August 16, 1949, was 1,021, 1,023, and 1,016. Results of urinalysis were normal. The urea nitrogen content of the blood was 16 mg. per 100 cc. The left kidney was poorly visualized in an intravenous pyelogram.

When last observed, five and a half months after operation, the patient was completely asymptomatic and was working eight hours a day. Blood pressure with the patient sitting

Chart 3.—Postoperative test with benzodioxane showed elevation of blood pressure, suggesting complete removal of pheochromocytoma. Response was one usually seen in essential hypertension.



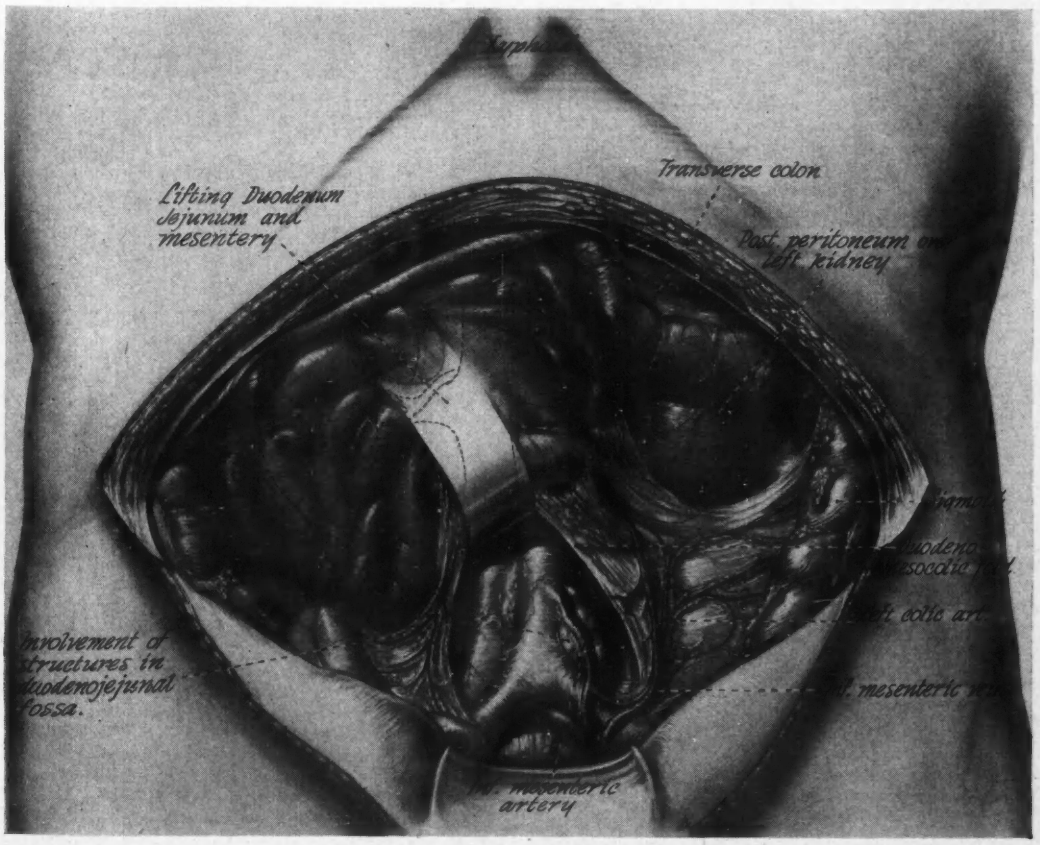


Figure 3.—Artist's conception of bilateral subcostal incision for exploration of suspected tumors of Zuckerkandl's bodies.

was 120 mm. of mercury systolic and 85 mm. diastolic; with the patient standing, 140 mm. and 100 mm. respectively. The slight hypertension which has persisted is probably secondary to the renal damage which occurred prior to the removal of the pheochromocytoma.

DISCUSSION

In most exploratory operations for adrenal tumors of this type, a posterolumbar incision has been used. The bilateral posterolumbar incision described by Young has been employed at times when the location of the tumor was uncertain before operation and when a tumor was not found associated with the adrenal gland first exposed. Other surgeons have preferred to perform the adrenal exploration transperitoneally through an incision in the anterior abdominal wall. Brunschwig, Humphreys and Roome[2] favor the anterior abdominal incision for the following reasons: "(1) Multiple tumors may be present, (2) There may be congenital absence of one adrenal gland, (3) Where, as in some reported instances, the tumor is on the anterior aspect of the kidney and adherent to surrounding tissues, sparing this kidney would be more feasible from an anterior approach than through a lumbar incision." Pneumoretroperitoneography for localization of the tumor is not without hazard and has not been used in many of the successfully treated cases. If localization of the tumor is not possible before operation, bilateral adrenal exploration is more readily performed through an anterior abdominal incision.

The benzodioxane test has been accepted in recent years as a relatively successful diagnostic procedure in cases in which pheochromocytoma is suspected. The efficacy of this drug was demonstrated in this case, not only in diagnosing the original condition, but also as a postoperative test to confirm the successful removal of the entire tumor. This drug has been employed as a diagnostic aid in examination of hypertensive patients at this hospital. No ill effect of the drug was observed in these studies. Drill[3] reported one case of nausea and headache and one in which precordial pain was noted following the use of the drug. The use of histamine injection as a diagnostic procedure is also considered to be hazardous because of the pronounced increase in blood pressure which may occur. Consequently, other drugs, such as tetraethylammonium bromide, are recommended in view of the fact that the blood pressure rise can be more easily controlled by postural changes.[6] The case described in this report again emphasizes the recessibility of many of the effects of a persistent elevated blood pressure, as is demonstrated by the pronounced improvement of the eyegrounds, in kidney function and in electrocardiogram tracings. Similar improvement has been noted by others (Bruce, Brunschwig, Kvale).

SUMMARY

A case of pheochromocytoma in a 37-year-old male who had typical attacks of paroxysmal hypertension, is reported. The diagnosis was confirmed by the use of benzodioxane and histamine tests.

A transverse upper abdominal incision was found to give adequate exposure for bilateral exploration of the adrenal glands and removal of the tumor.

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Dermoid Cyst of the Omentum

With Report of a Case

HOWARD B. KIRTLAND, JR., M.D., *San Diego*

IN a recent article dealing with omental cysts of clinical importance, Beahrs and Dockerty reviewed the literature on omental tumors and added 14 previously unreported cases of omental cysts. They divided omental tumors into solid and cystic. The cystic outnumbered the solid tumors in a ratio of 4 to 1. The malignant solid liposarcomas and fibrosarcomas were more frequent than the benign lipomas. Cysts of the omentum were subdivided into pseudocysts and true cysts. As examples of pseudocysts they cited cystic lesions following fat necrosis, those forming at the site of trauma with hematoma, those caused by reaction about a foreign body (such as gauze or petrolatum) and, most common, hydatid cysts. The true cysts were usually lined with epithelium or endothelium. Dermoid cysts, of which perhaps a dozen have been reported in the literature, were said to be examples of the epithelium-lined true cysts. Cysts which are probably congenital lymphangiomas but which might be the result of imperfect fusion of the opposed omental surfaces were cited as typical endothelium-lined cysts. Beahrs and Dockerty pointed out that the fewer than 100 cases of omental cysts in the literature probably did not represent the true incidence. The reported age range of patients was 3 months to 76 years, the majority of cysts occurring in the early years of life, 68 per cent among patients less than 30 years of age. Sixty per cent occurred in females. There was no racial predilection. The cysts were asymptomatic or the symptoms were caused by the size of the lesion, rupture of the cyst or torsion of the pedicle.

The following report of a case of dermoid cyst of the omentum is presented because the patient was older than any previously reported, because of the acute symptoms that were present owing to torsion and infarction, and because of the clinical and roentgenologic observations.

A 78-year-old white woman was admitted to the San Diego County General Hospital with a four-day history of shooting pain in the lower abdomen. The pain was intermittent but recurred with increasing frequency and severity. Marked anorexia developed on the day of entry. The

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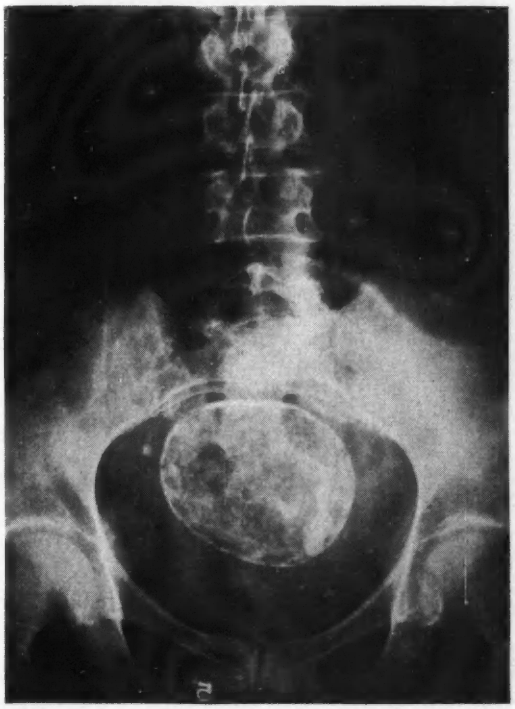

Figure 1.—Roentgen appearance of dermoid cyst of the omentum.

patient had not had similar attacks previously. There were no other symptoms referable to the gastrointestinal or genito-urinary tracts. Heart disease of long standing had responded well to treatment.

The temperature was 99.6° F., the pulse rate 100, and respirations 28 per minute. The blood pressure was 200 mm. of mercury systolic and 110 mm. diastolic. The abdomen was protuberant and soft with some voluntary guarding and spasm in the lower two-thirds where there were generalized tenderness and rebound tenderness. Peristalsis was hypoactive. In pelvic and rectal examinations severe pain was elicited by motion of the cervix. In a roentgenogram of the abdomen early ileus and what was interpreted as a large calcified leiomyoma were noted (Figure 1). A clinical diagnosis of infarcted leiomyoma of the uterus was made.

At operation a hard, purplish-red tumor, 10 cm. in diameter, was observed. It contained areas of necrosis and was surrounded by fresh adhesions. The tumor arose from the omentum and lay in the lower abdomen and upper pelvis. The omental pedicle had rotated through three complete turns, and was infarcted. There was no evidence of ovarian attachment. A small amount of free blood was present in the abdomen. Removed and sectioned, the tumor was observed to be a hair-filled dermoid cyst of the omentum with a heavily calcified wall.

The postoperative course was uneventful. The patient was discharged asymptomatic and ambulatory on the sixth postoperative day.

2120 Fourth Avenue.

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Bronchiogenic Cysts

A Report of Two Cases

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AGE extremes for bronchiogenic cysts are well illustrated by the following two case reports, which are considered to be of special interest in that they show some variation in clinical manifestations and anatomical location. Although the lesion is relatively rare, several series of cases have been reported. In 1945, Laipply[2] reported a total of 35 cases collected from the literature. The following year, Blades[1] reported upon an additional 23 cases of bronchiogenic cysts observed in army hospitals, and several small series have been reported since.

These cysts usually arise at or near the tracheal bifurcation. Embryologically, the primitive foregut divides longitudinally, forming the trachea anteriorly and the esophagus posteriorly. Cyst formation is most frequent at the lowest point of division. Histologically, the cyst usually contains elements of the bronchial wall; however, gastric or esophageal derivatives may be present. Cyst formation is thought to be due to the pinching off of a diverticulum at the carinal level or more distally along the main stem bronchi as development proceeds. Due to variations in growth, cysts may be solely mediastinal in position or intimately associated with the fissures or lung parenchyma.

Bronchiogenic cysts are usually detected on routine chest x-rays, for they seldom produce symptoms sufficient to cause the patient to seek medical aid. The principal clinical symptom, if any is present, is dull substernal pain, with or without cough. Wheezing or dysphagia may occur if there is partial obstruction of the trachea or esophagus. Cysts adjacent to the carina are likely to cause these symptoms in infancy or early childhood due to compression of the soft tracheal rings or impingement of the esophagus against the vertebrae. Such severe symptoms are seldom present if the cyst is located farther along a main stem bronchus. With severe bronchial compression, symptoms of atelectasis and pneumonia may ensue. The presence of infection may also indicate the existence of a bronchial communication; the symptoms characteristic of lung abscess or other pulmonary infection would then occur.

In posterior-anterior x-ray films a bronchiogenic cyst appears as a rounded, fairly sharply circumscribed area of increased density near the midline, usually in the vicinity of the hilum. Such lesions are more often on the right side than on the left (Figures 1 and 2). A bronchial communication with the cyst, which is rare, may permit air to enter and, at times, show a fluid level. In the lateral x-ray view the cyst is usually seen in the central mediastinum, either posterior or anterior to the trachea (Figures 1 and 2). If the lesion is large, compression of contiguous structures

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may be observed. Bronchograms may be helpful in showing bronchial distortion or obstruction. If there is an opening into the bronchus, introduction of a contrast medium may delineate the interior of the cyst. Planigrams may sometimes show the bronchial encroachment. Fluoroscopy may show movement of the mass on swallowing, which would suggest a tracheal attachment. If the cyst is anterior and near the pulmonary artery, angiograms may be used to exclude vascular tumor in differential diagnosis. If there is no encroachment of the cyst on a major bronchus, the lesion may not be observed in bronchoscopic examination. Pressure may cause mucosal edema or displacement of the bronchi. Complete bacteriologic and cytologic examination of the sputum discloses no diagnostic information relative to bronchiogenic cysts.

The following two cases of a relatively rare lesion, one in an elderly woman and the other in a young girl, were brought to the authors' attention within a one-week period:

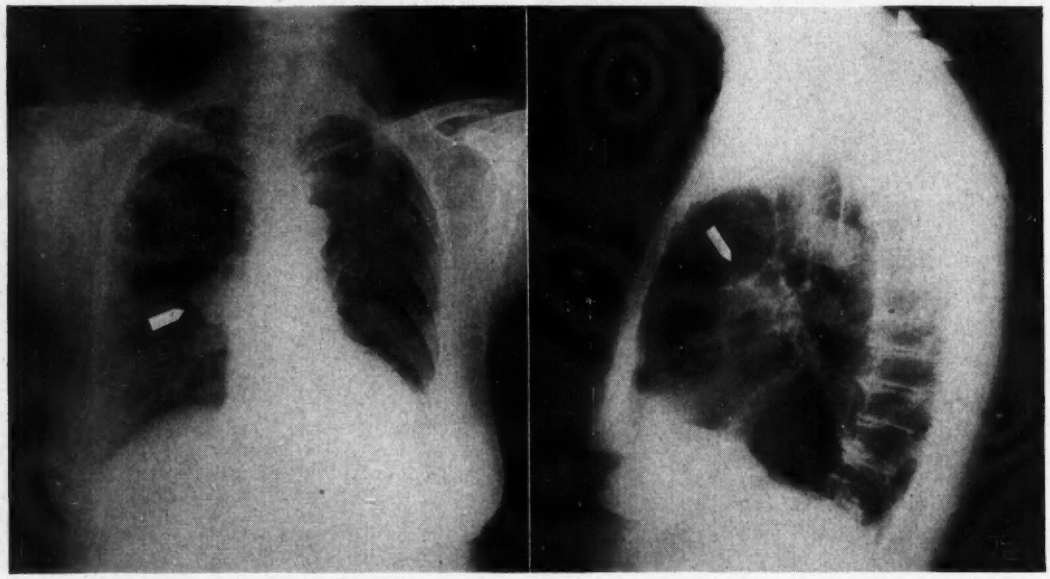

Figure 1.—*Left*—Bronchiogenic cyst present in right hilar area in 75-year-old female. *Right*—Right lateral view of the same patient, showing the cyst anteriorly in the right hilum.

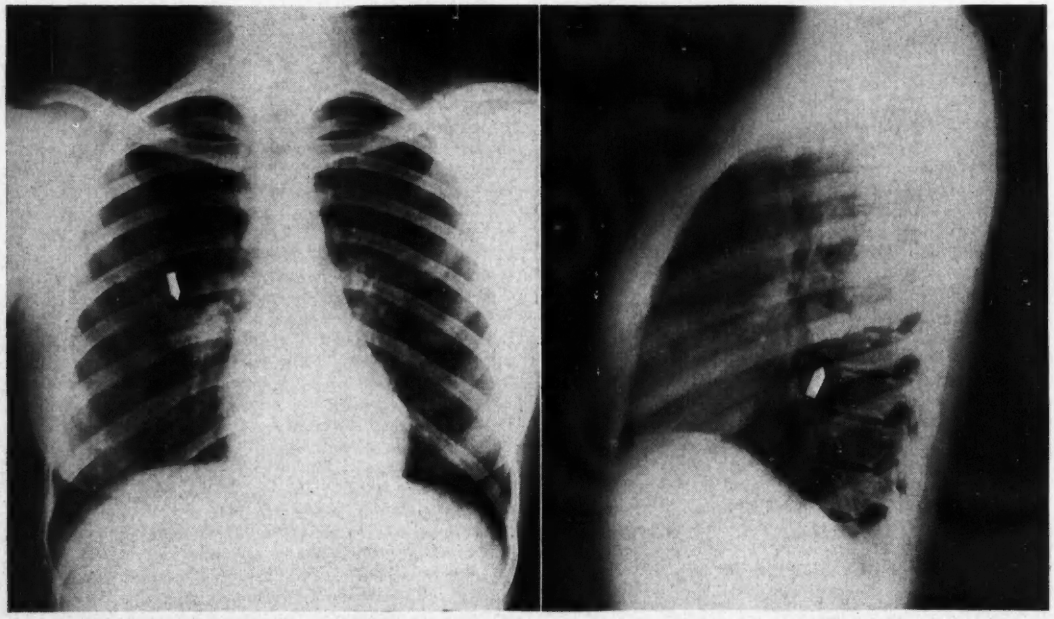

Figure 2.—*Left*—Bronchiogenic cyst present in right hilar area in 20-year-old female. *Right*—Right lateral view of the same patient showing the cyst posteriorly in the right hilum.

CASE 1: A 75-year-old white woman felt well until August 10, 1950, when a common cold developed. It gradually subsided except for mild residual cough. No abnormality was noted on physical examination. The blood pressure was 180 mm. of mercury systolic and 90 mm. diastolic. Results of urinalysis were within normal limits, and the blood was normal except for mild normocytic hypochromic anemia. In x-ray films of the chest (Figure 1) a circular mass was noted in the right anterior hilar area at the root of the right lung. Full excursion of the tumor mass on inhalation and exhalation was observed fluoroscopically. In bronchoscopic examination the right main stem bronchus was observed to contain a small amount of mucus. At the level of the superior segmental branch and the middle lobe orifice there was slight edema and pallor. In biopsy of a specimen taken from this site, mild inflammatory reaction was noted. Exploratory thoracotomy on the right side was carried out two months after the onset of symptoms. The tumor was cystic, ovoid in shape and 3 x 4 cm. in size. Inferiorly, it was adherent to the pulmonary artery and at the hilar end was adherent to the right main stem bronchus. It contained a viscid, brownish-black fluid with a slightly greenish cast. After evacuation, the cyst lining was white, smooth and glistening, and two small spicules of cartilage were noted within the sac wall. The cyst was freed from the upper and middle lobes down to the hilum. It was fused to the pulmonary artery and the intermediate bronchus. Most of the sac was excised and the margins were closed to obviate the formation of a bronchopleural fistula. Recovery was uneventful.

Pathologic Report: The interior of the cyst was in part lined by flattened bronchial epithelium. Smooth muscle was scattered throughout and in one area a portion of cartilage was encountered. Beneath the lining epithelium, old hemorrhage was indicated by an accumulation of hemosiderin pigment bearing macrophages. There was no evidence of malignancy in the sections examined.

* * *

CASE 2: A 20-year-old girl, entirely asymptomatic, had an x-ray film of the chest taken in a survey program in August 1950. Family and past history were irrelevant. Physical examination was normal. In x-ray films (Figure 2) a density in the right posterior hilar area was noted. Results of laboratory studies were normal. In bronchoscopic examination the tracheobronchial tree was observed to be normal, with a small amount of gray mucus in the right main stem bronchus. Microscopic examination of the bronchial aspirations showed normal bronchial epithelium; no malignant cells were observed.

The right chest was explored in October 1950. Deep in the long fissure between the lower and upper lobes, a soft cystic ovoid mass, measuring 3 x 4 cm. in diameter, was freed on all sides from the vessels and lung tissue. The capsule was yellowish-white in color and the thin, syrupy contents were a translucent white. The base of the cyst was adherent to the superior segmental bronchus. In removal of the cyst, the bronchus had to be divided, so resection of the superior lobar segment of the right lower lobe was carried out. Recovery was uncomplicated.

Pathologic Report: The cyst wall varied in thickness from 1 to 2 cm. and contained a thin, gelatinous, turbid fluid. The lining epithelium was stratified columnar and several small scattered glands were present beneath it. Cartilage and smooth muscle were present. There was no evidence of malignancy.

DISCUSSION

The coincidental occurrence of these two cases permitted detailed comparisons. In the 75-year-old patient, the cyst was located in the anterior right hilum with the attachment proximal to the middle lobe bronchus. The cyst lay in the short fissure between the upper and middle lobes, anteriorly (Figure 1). The younger patient also had a cyst in the right hilar area, but it lay in a posterior position and was attached to the superior segmental bronchus of the right lower lobe (Figure 2). The cysts in these two cases were almost exactly the same size, and both were ovoid. In the case of the younger patient the cyst was completely asymptomatic. In the elderly woman, symptoms were of two months' duration, so the conjecture of hemorrhage initiating symptoms must be considered. In this case the cyst contained fragments of cartilage perforating the inner lining of the thin wall, as well as a dark brown oily liquid identical in appearance to the contents of pelvic chocolate cysts in endometriosis. In the case of the young woman the cyst contained a white somewhat translucent mucilaginous material. Sections of the wall of the cyst in both cases showed the usual structures found in a bronchial wall. The lining surface of ciliated columnar epithelium was smooth and in one instance a tendency to trabeculation was present in the distal portion. Mucus glands, cartilage, elastic tissue and smooth muscle were present in each. Cartilage was in minimal amounts with no tendency to ring formation.

In the absence of infection, as was true of these two cases, symptoms were dependent upon the size and location of the mass. In the young patient, no degree of questioning gave the least suggestion of any symptoms prior to incidental discovery of the lesion on a routine chest x-ray. In the elderly patient there were no symptoms prior to the onset, two months earlier, of cough and associated chills and fever. One might surmise that the beginning chill and cough followed the hemorrhage into the cyst which caused very rapid swelling and compression of adjacent lung tissue. The bronchoscopic observation of edema of the mucosa adjacent to the middle lobe orifice suggests this sudden encroachment.

DIAGNOSIS AND TREATMENT

An absolute diagnosis is seldom made without operation or autopsy. Certain roentgenologic and clinical features suggest a probable diagnosis prior to operation. In both of the cases reported here, the diagnosis of bronchiogenic cyst was considered most likely preoperatively, chiefly on the basis of x-ray evidence. The cysts usually lie somewhat posterior but adjacent to the hilar areas and not in the paravertebral area where tumors of nerve origin are most common. Substernal tumors or anterior mediastinal masses are usually thymic, thyroid or teratodermoid in type. Differentiation from a malignant neoplasm can seldom be made clinically. In the treatment of these lesions, exploration should be carried out and the cyst removed in entirety if possible. Carcinomatous change has been known to take place in the epithelial lining of bronchiogenic cysts, although this is unusual. With present-day techniques, plus chemotherapy, it is relatively safe to open the chest, inspect the lesion or remove any tumor mass. In the two cases reported a posterior lateral approach was used.

SUMMARY

Two cases of bronchiogenic cyst, one in a girl 20 years of age, the other in a woman aged 75, are reported. The problems in diagnosis are presented and the necessity of performing an exploratory thoracotomy to rule out a malignant tumor is emphasized.

1441 Westwood Boulevard.

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Circumcaval Ureter

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SINCE Hochstetter's[7] report in 1893 on the dissection of an infant, reports of cases of circumcaval ureter have been frequent enough to remove this lesion from the list of exceedingly rare anomalies.

Duff,[4] in a review of the literature in connection with a case reported by him in 1950, gathered reports of 39 cases. In 22 instances the abnormality was noted in the anatomical laboratory or at necropsy, in 13 it was observed at operation, and in four instances was diagnosed preoperatively. Surgical repair was carried out in nine cases, with good results in seven. De Carlo[3] observed circumcaval ureter in one of 4,185 cadavers dissected at the Daniel Baugh Institute of Anatomy.

For practical purposes circumcaval ureter may be regarded as a right-sided anomaly. (The only case of bilateral retrocaval ureter in the literature was reported in 1905 by Gladstone[5] who, in dissecting the body of an infant, observed postrenal vena cava on both sides.) The lesion occurs as the result of the persistence beyond fetal life of the posterior cardinal vein, which is the primitive vein for the posterior part of the body. Ordinarily the inferior vena cava is formed by the union of that part of the vena cava which is cephalad to the kidney and the iliac veins at their junction, and the cardinal vein then atrophies. When this atrophy does not take place the cardinal vein becomes the main channel of the inferior vena cava and the ureter must of necessity pass behind it. Thus, it is a vascular and not ureteral anomaly.

The embryological aspects of circumcaval ureter have been gone into exhaustively by McClure and Butler,[9] Gruenwald and Surks,[6] Randall and Campbell,[12] Pick and Anson[11] and Wilson and Herzlich.[13]

When conditions permit, the treatment, as reported by Kimbrough[8] in 1934, is to divide the ureter, bring the distal end over the vessels and anastomose the severed ends. In most cases the ureteral obstruction has caused such a degree of renal damage that nephrectomy is imperative.

Recently, Beard and Goodyear[1] suggested two procedures which should be of assistance in making a precise diagnosis. In one of two cases reported by them a venacavogram was made after the method of O'Loughlin.[10] (Twenty cubic centimeters of a 35 per cent solution of Diodrast® is injected into the femoral vein. This outlines the iliac vein and the inferior vena cava. If a denser shadow is desired, 70 cc. can be injected without harm.) In the other case a No. 8 catheter was passed into the antecubital fossa to the heart and down the vena cava. With the vena cava thus outlined and radiopaque catheter in the ureter in question, stereoscopic films were taken, making the relations of the ureter and vena cava plain.

Randall and Campbell suggested that in a lateral view with a ureteral catheter in place, if the ureter is postcaval the catheter will appear to impinge on the vertebral column while the normally situated ureter will fall away. (In oblique views in the case herein reported, this impingement was observed.) Creevy[2] expressed the opinion that failure to identify the lesion by pyelography must be due to unfamiliarity with the condition, since the course of the ureter is so typical that once seen it is not easily forgotten. The author is in complete accord with this statement. In illustrations printed with several reported cases the films so closely resemble one another that a casual observer might take them all for pyelograms in a single case.

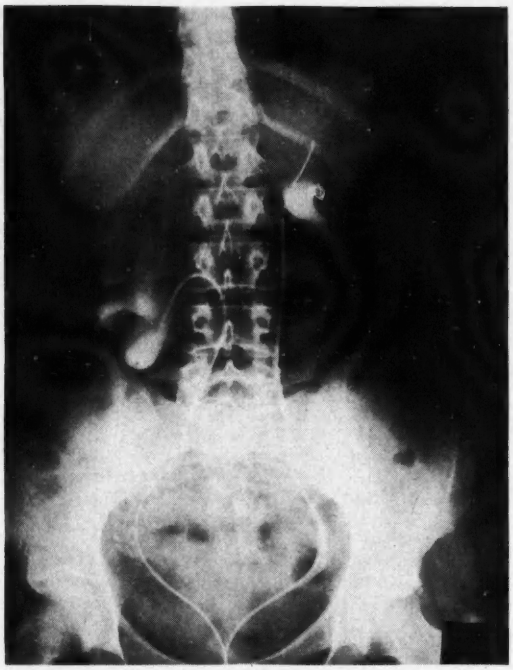

Figure 1.—Preoperative film showing course of ureter.

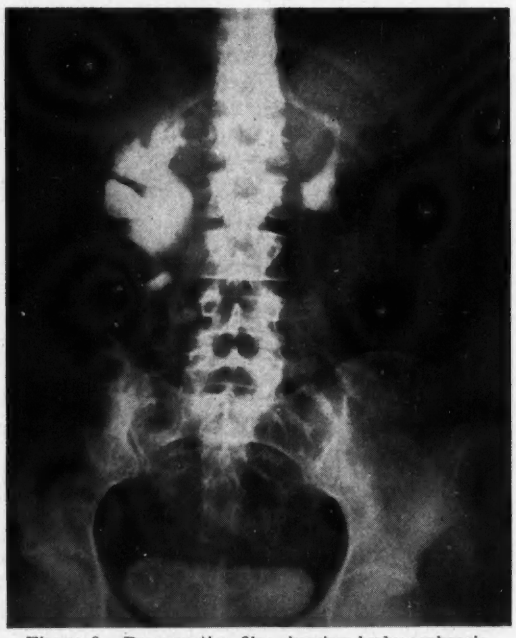

Figure 2.—Preoperative film showing hydronephrosis.

REPORT OF A CASE

The patient, a white woman 35 years of age, stated that in November 1947 she ran a nail into the left great toe and the toe became infected. Chills, fever and a pain in the right side of the back followed. In an intravenous pyelogram an obstruction on the right side with no evidence of calculus was observed. There was considerable distention of the pelvis of the kidney with some blunting and irregularity of the calices. A week later cystoscopy and retrograde pyelography were done. The ureteral orifices were normal in location and

appearance. No. 5 catheters were passed to both renal pelves without meeting obstruction. Urine dropped continuously from the right ureter and intermittently from the left. Indigo carmine injected intravenously appeared in good concentration and in normal time on the left, and in fair concentration and in normal time on the right.

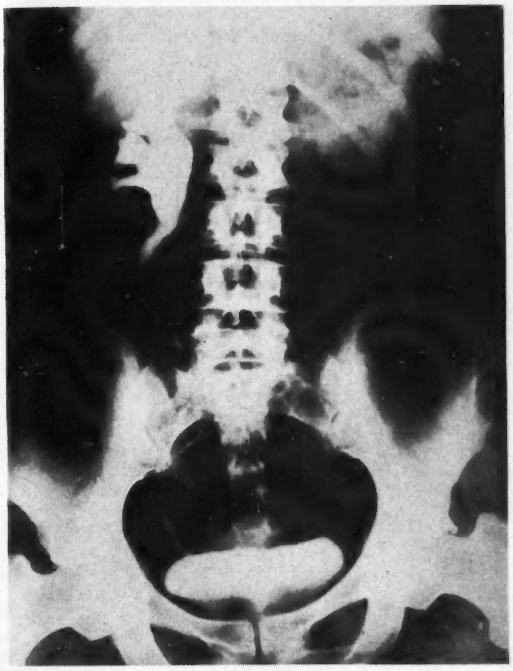

Figure 3.—Film two years postoperatively.

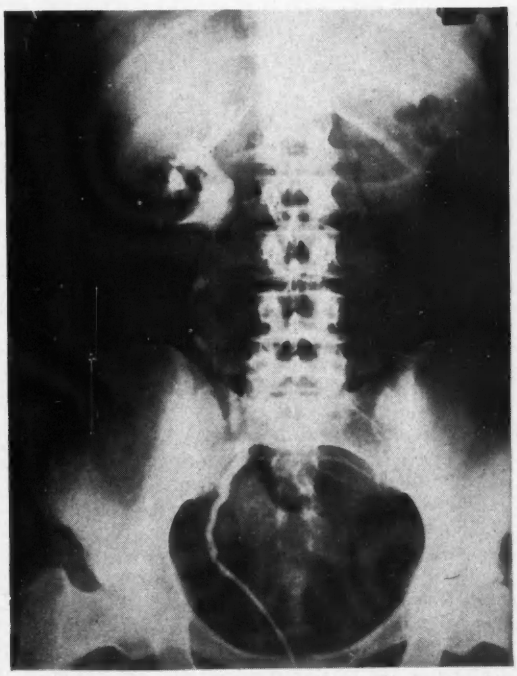

Figure 4.—Twenty-six months postoperatively, showing further shrinkage of pelvis.

Plain films, and pyelograms, supine, erect and right oblique, were taken. There was evidence of a considerable degree of hydronephrosis on the right. The upper ureter was quite redundant, forming a long curve. It extended first downward from the ureteropelvic junction, then upward and mesially for about three inches. The portion described was quite wide and the hydronephrosis was apparently caused by a kink at the level of the third lumbar vertebra.

The patient entered Providence Hospital on March 4, 1947, with a diagnosis of hydronephrosis, hydroureter and circumcaval ureter on the right side.

A right loin incision was made. The upper two-thirds of the right ureter and the lower pole of the right kidney were exposed. The ureter was observed to course under the inferior vena cava and to reappear below the division of the right common iliac. To clear the field, the right ovarian vein was ligated. The ureter was then sufficiently freed above and below so that traction on the ureter did not affect the vessels. The ureter was then divided at right angles to its long axis above the vena cava and the distal portion was pulled from under the vessel and then brought over the iliac vessels and vena cava. About 2 cm. of the redundant ureter was excised and the ureter was then anastomosed with number 4-0 chromic, interrupted sutures on an atraumatic needle. A No. 10 T tube was used both as a splint for the anastomosis and as a drain for the pelvis. It was introduced into the ureter 2 cm. above the site of the anastomosis. The kidney, which was not mobile, was not disturbed in its bed.

Three days postoperatively the patient became afebrile. She was discharged on the 12th day. The T tube was removed on the 25th day. At that time there was no return of indigo carmine from the right kidney. One month later there was still no dye from the right side but the orifice was observed to contract and dilate in a normal manner. The second month after the T tube was removed the dye appeared in good concentration 25 minutes after it was injected. After that the function of the right kidney, as measured by the intravenous injection of indigo carmine, was normal, the dye appearing in 5 to 7 minutes in good concentration. The right ureter was dilated nine times the first postoperative year and then let alone.

At two years and at 26 months postoperatively pyelograms were taken. The hydronephrosis was observed to be largely relieved. In a film taken ten minutes after the pelvis was filled and the catheter withdrawn it was noted that in the erect position the pelvis emptied normally. The urine was never grossly contaminated. Penicillin and sulfadiazine given for several days before the operation had rendered the urine free from pus and organisms and it remained so afterward. After the operation the patient worked and lived in a normal manner.

COMMENT

The success or failure of plastic operations on the kidney pelvis and ureters appears to depend to a large extent on the degree of infection, and, to a scarcely less extent, on the patient's intelligent cooperation. An important feature in the case presented was that the diagnosis was made preoperatively, which permitted the planning of the operation. The plastic T tube, used both as a splint to the ureter and a drain for the pelvis, apparently fulfilled these two duties satisfactorily.

SUMMARY

A circumcaval ureter was diagnosed preoperatively on the basis of roentgen evidence.

The preoperative diagnosis permitted careful planning of the surgical procedure. Anastomosis was done, using a T

tube both as a splint for the anastomosis and as a drain for the renal pelvis. Improvement in the kidney was observed pyelographically two years after operation.

3115 Webster Street.

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EDITORIALS

A New Study of C.P.S.

California Physicians' Service will be given another look-over in the coming year as a result of action taken by the C.P.S. House of Delegates at the annual meeting. The House adopted a resolution calling upon the Council of the California Medical Association to appoint a committee "to ascertain the expectations of the medical profession of California in regard to C.P.S."

The functions of this committee are given in the resolution as follows: ". . . to make a careful study of C.P.S. as related to the operations of private insurance companies and other prepaid medical care groups, and to determine the future role and purpose of California Physicians' Service in the whole field of voluntary prepaid medicine."

While the language of the resolution is permissive in "urgently requesting" the C.M.A. Council to appoint such a committee, the Council has acted in the spirit of the proposal and has taken steps to appoint a committee which will be representative of all sections of the state and of all interests of physicians in various types of practice.

Appointment of this committee, which is expected to start functioning immediately, is reminiscent of the "Chandler Committee" of 1945-46. That group resulted from a similar demand from the House of Delegates for a scrutiny of medicine's own prepayment plan; its purpose was somewhat different from that of the present committee, in that it aimed primarily at going into the business affairs of C.P.S., particularly as those affairs affected the relationship between the organization and its physician members. At the same time, many of the considerations of the earlier committee will doubtless be given further study by the present body.

If the findings, recommendations and results of the "Chandler Committee" study may be taken as a criterion, the review of C.P.S. by the present committee should have a salutary effect. The former committee made a series of recommendations which were put into effect by C.P.S. and the C.M.A., including: Recognition of a system of both service and indemnification, with an income ceiling as the dividing line; biennial revision of the C.P.S. fee schedule; recognition of the need for periodic revision of the income ceiling; recognition of the need for C.P.S. to make its own hospitalization arrangements; approval of surveys of the business methods of C.P.S.; recognition of the respective spheres of authority of the C.M.A., the C.P.S. Board of Trustees and the management executives of C.P.S.; appointment of competent businessmen to the Board of Trustees of C.P.S. and, finally, continued sponsorship of C.P.S. and the voluntary systems of prepaid medical care by the California Medical Association.

There were additional recommendations of a more technical nature but the results of the foregoing may all be seen in the current operations of C.P.S.

The current committee will be looking into the entire picture of C.P.S. from a little different angle but still from the point of view of the practicing physician. Voluntary health insurance has grown so rapidly, and competition today is so keen among the numerous underwriters, that an attitude of let's-stop-and-take-stock is dictated by sound judgment. An appraisal of the place of C.P.S. in the sun of voluntary health insurance cannot but be helpful to the medical profession. An unbiased study of its "future role and purpose" will undoubtedly result in a clear picture of just where medicine's baby is going and should go. At the same time, the committee will have a chance to take a closer look at other

forms of voluntary prepaid medical care and to assess them at their true value and their comparative status with C.P.S.

The functioning of this committee in the coming year will mark another step forward in the search for truth in the important field of voluntary prepaid medical care. The American public, and especially the California public, has made its wishes crystal-clear in demanding that *some* system of health insurance be available. If the medical profession is to maintain its leadership in properly appraising and meeting the public interest, an objective review of the current situation is bound to be helpful.

The new committee has a big job cut out for it. In prospect, it looks as though the committee can and will handle its work in capable fashion and will come up next year with ideas which will be beneficial to all concerned, including physicians.

A.M.A. 1951 Meeting

Atlantic City, with its huge exhibit hall and rows of large boardwalk hotels, last month played host to the 100th Annual Meeting of the American Medical Association, a meeting which was marked for its quiet and calm. In earlier years some A.M.A. sessions have covered some bitterly controversial subjects in the policy-making House of Delegates. In contrast, the 1951 meeting accomplished its business with a minimum of argument and a maximum of speed.

With the close of the session, it appeared that California had carried off at least its share of the honors. Dr. John W. Cline was installed as president of the A.M.A., Dr. Dwight H. Murray was elected Chairman of the Board of Trustees and Mrs. Ralph B. Eusden was elected President-Elect of the national Woman's Auxiliary. On top of that, three Californians were named by their specialty sections as members of the House of Delegates, increasing the California strength in the House to 14 out of 201 members.

Immediately preceding the A.M.A. meeting, the annual session of the American College of Radiology bestowed upon Dr. Lowell S. Goin, a former C.M.A. president, its coveted Gold Medal for outstanding achievement in the field of radiology. Doctor Goin is the first recipient of this award since 1941 and the seventh in the history of the College. As such he follows in the footsteps of Mme. Curie and other renowned figures in the development of radiology.

Tackling the question of the dual system of membership and fellowship in the A.M.A., the House of Delegates voted to put over final consideration until the interim session next December. This confusing situation should be straightened out at the earliest possible moment; in the light of existing policies of the A.M.A. in collecting annual dues from its members, the classification of fellowships seems to be an unneeded appendage which could easily and profitably be excised. The business offices of every medical society would favor such a move, as well as the individual members who are caught up in the tangle of duplication of effort without tangible benefit.

The House of Delegates took positive action on the question of hospital accreditation, by approving the action of the Board of Trustees of agreeing to participate in a program in which the official accrediting body would be composed of representatives of the A.M.A., the American College of Surgeons, the American College of Physicians and the American Hospital Association. Hospital inspection under this program would be rotated among the representatives of the several groups.

Next December's meeting of the A.M.A., the clinical session, will be held in Los Angeles, which then for the first time will have a chance to play host to the national body. The 1954 Annual Session will be held in San Francisco, a decision which was unanimously voted.

It may be true, as some wag stated, that in ten years nobody will even know that the A.M.A. held a meeting in 1951; on the other hand, the scientific advances of the meeting bear tribute to medicine's ever-progressive attitude, even though the business side of the meeting may have been without great incident.

CALIFORNIA MEDICAL ASSOCIATION

NOTICES AND REPORTS

The C.M.A. President-Elect

Lewis A. Alesen, M.D., comes to the high office of President-Elect of the California Medical Association with an unusual apprenticeship and training in medical executive positions.

Dr. Alesen was born in West Pullman, Illinois, December 4, 1896. At the University of Illinois he received his Bachelor of Science degree in 1919 and a doctorate in medicine in 1921. He took his hospital training at the Los Angeles County Hospital. Dr. Alesen began the private practice of medicine in 1923. He is a diplomate of the American Board of Surgery and a fellow of the American College of Surgeons and of the International College of Surgeons. For many years he has been Associate Professor of Surgery at the College of Medical Evangelists.

Early in his medical career Dr. Alesen became interested in organizational work. One of the founders of the old Fellowship Club (later to become the Junior Section), he represented this group in the Council of the Los Angeles County Medical Association in 1934. He was a Councilor in that body until 1940. In that year Dr. Alesen became secretary-treasurer of the Los Angeles County Medical Association, served in that position for three years, and was elected president in 1944. He is a member and a past president (1949) of the Los Angeles Surgical Society. He has been chairman of the Department of Surgery at the Los Angeles County Hospital since 1949.

In 1945 Dr. Alesen was elected Vice-Speaker of the House of Delegates of the California Medical Association, a position in which he served for two years under the able guidance of Dr. E. Vincent Askey. Advanced to the position of Speaker in 1947, he served with distinction in that capacity until his elevation to the office of President-Elect this year. Dr. Alesen is also a delegate to the House of Delegates of the American Medical Association.

Dr. Alesen has always stood resolutely for the dignity of the private practice of medicine. While he is proud to be classed as a "rugged individualist," he is far from being a reactionary. He is firm in his conviction that the profession of medicine can and will resolve the problems which confront it in the complexities of present-day society. He has no delusions that this goal may be reached by wishful thinking and he brings to his new task a fighting spirit, a clear-thinking mind and a devotion to the ideals which have made American medicine and the American nation the greatest in the world.

LEWIS A. ALESEN, M.D.

Dr. Murray Heads A.M.A. Board of Trustees

California was signally honored by the American Medical Association this year when, at the close of the A.M.A. annual session, Dr. Dwight H. Murray of Napa was unanimously elected Chairman of the A.M.A. Board of Trustees.

Doctor Murray has long been known to the medical profession in California as an untiring leader, especially in the field of medical legislation. In more recent years he has attained the same position in the national legislative field and for several years past has served as chairman of the legislative committee of the A.M.A. Board of Trustees.

Born in Indiana in 1888, Doctor Murray was graduated at the University of Indiana School of Medicine in 1917. Almost immediately he went into active service with U. S. Navy, serving in the Atlantic under Admiral "Bull" Halsey and other commanders whose names have since become famous. Upon his release from the Navy in 1921, he established a general practice in Napa and has remained there to this time.

Dwight Murray, "Murph" to his friends, displayed an interest in legislative activities in California a number of years ago and in 1940 was appointed chairman of the C.M.A. Committee on Public Policy and Legislation, a post he has filled most capably from that time on. In late 1944 he was the guiding force behind establishment of the United States Health League, a coalition of western states medical associations which opened medicine's first legislative representative office in Washington, D.C. He has served as chairman of that group from its inception.

Recognition of Doctor Murray's extensive legislative knowledge came in 1945, when he was elected a member of the A.M.A. Board of Trustees, succeeding the late Edward M. Pallette of Los Angeles. His work on the top A.M.A. board was described by a national magazine some time later in a series of thumbnail personality sketches of the board members; the magazine said in effect that "Doctor Murray sits back quietly, waits until all the arguments are in and then busts loose and gives 'em hell."

As California's legislative chairman for the past 11 years and as A.M.A. legislative chairman for the past three years, "Murph" has repeatedly proved his great capabilities beyond shadow of doubt. It is certain that in his new capacity as board chairman he will rise to new heights as a leader in the American Medical Association and as an effective spokesman for the medical profession.

Doctor Murray resides in Napa, is married and the father of two children. His daughter Jean is married to Robert Huber, a young San Francisco attorney, and is the mother of two children. His son, "Mike," is a freshman medical student at University of California School of Medicine.

Only one question remains unanswered about Dwight Murray. How can he do as much as he does and still carry on an extensive general practice? The answer doubtless lies in his great capacity for friendship and for getting things done with a minimum of difficulty. The best portrait of Dr. Murray is the esteem in which his patients, as well as his colleagues, hold him.

DWIGHT H. MURRAY, M.D.

Council Meeting Minutes

Tentative Draft: Minutes of the 379th, 380th, 381st, 382nd and 383rd Meetings of the Council of the California Medical Association.

379th Meeting

The meeting was called to order by Chairman Shipman in Conference Room 8 of the Biltmore Hotel, Los Angeles, at 9:30 a.m., Saturday, May 12, 1951.

Roll Call:

Present were President Cass, President-Elect MacLean, Speaker Alesen, Vice-Speaker Charnock, Councilors Shipman, Lum, Ball, Crane, Henderson, Dau, Ray, Montgomery, Pollock, Green, West, Heron, Thompson and Bailey, Secretary Daniels and Editor Wilbur. Absent for cause: Councilor Frees.

Present by invitation were Executive Secretary Hunton, Legal Counsel Hassard, Field Secretary

Clancy, Public Health League of California Executive Secretary Read, Dr. Robertson Ward of California Physicians' Service, Legislative Chairman Dr. Dwight Murray, county society executive secretaries Waterson of Alameda-Contra Costa, Wood of San Mateo, Donovan of Santa Clara, Gillette of Fresno, Venables of Kern, Cochems of Los Angeles and Tobitt of Orange, Public Relations Counsel Clem Whitaker, Jr., Ned Burman and James Dorais.

Present by invitation during parts of the meeting were Dr. John W. Cline, president-elect of the American Medical Association, Orris R. Myers of Humboldt County and Joseph Josephson of Santa Clara County.

1. *Minutes for Approval:*

On motion duly made and seconded, minutes of the 378th Council meeting, held March 17, 1951, in San Francisco, were approved.

2. *Membership:*

(a) A report of membership as of May 5, 1951, was received and ordered filed.

(b) On motion duly made and seconded, 2,171 members whose dues had been received since April 1, 1951, were voted reinstatement as active members.

(c) On motion duly made and seconded in each instance, 26 applicants were elected to Associate Membership. These were:

Henrik L. Blum, Eva Haumeder, Carl C. Epstein, Lowell E. Kidder, William James Perry and William W. Stiles, Alameda-Contra Costa County; J. C. Drake and Ira J. Seitz, Fresno County; Alvin R. Leonard, San Diego County; Louis Brizzolara, Ellen Brown, Herbert Dryfoos, Z. L. Henry, R. S. Sherman, Jr., and Pearl M. Smith, San Francisco County; Doris Abrams, A. V. Giampaoli, Gordon Helsley, William Jepson, Louise Smith King and John Lane Pasmore, Santa Clara County; Marshall Porter, Sonoma County; Michael T. Koenig, Wm. E. McCullough, Walter P. Streitel and Adolf Wallner, Ventura County.

(d) On motion duly made and seconded in each instance, five applicants were elected to Life Membership. These were:

J. O. Chiapella, Butte-Glenn County; Joseph R. Allen and James M. Stoddard, Los Angeles County; George H. Cruikshank, San Diego County; Harry R. Oliver, San Francisco County.

(e) On motion duly made and seconded in each instance, ten applicants were elected to Retired Membership. These were:

Richard G. Watson, Alameda-Contra Costa; Edwin R. Scarboro, Fresno County; Montrose M. Bernstein and C. F. Schmid, Los Angeles County; E. V. Knapp, Marin County; Burnett W. Wright, San Diego County; Samuel Hanson, San Joaquin County; W. H. Heuschele, Santa Clara County; Reo B. Armitstead and Arthur H. Stoll, Ventura County.

(f) On motion duly made and seconded in each instance, 21 applicants were granted reductions of dues because of postgraduate study or protracted illness.

3. *Financial:*

(a) A report of bank balances as of May 5, 1951, was received and ordered filed.

(b) A report of revenues and expenditures for April and for the ten months ended April 30, 1951, was received and ordered filed.

(c) Dr. Donald D. Lum, chairman of the Auditing Committee, presented a proposed budget for the fiscal year starting July 1, 1951. Several items came under discussion and adjustments from the proposed budget were agreed upon. On the basis of the proposed budget, the Council voted to recommend that dues for the calendar year 1952 be $40 per active member and that this figure and this budget be presented to the Finance Committee of the House of Delegates with the Council's recommendation for adoption.

4. *Committee on Industrial Accident Commission:*

Dr. Frank J. Cox, chairman of the Committee on Industrial Accident Commission, reported on a preliminary study made by an economist employed by the committee to investigate the level of industrial medical and surgical fees in their relationship to other economic factors. This study has shown that medical fees have lagged far behind other economic index factors over a period of years and that adjustments are indicated. He also reported on meetings held with representatives of compensation insurance carriers and with members of an interim committee of the State Legislature. Dr. Cox suggested that further studies be carried on under an appropriation of $15,000 previously granted his committee by the Council.

There was considerable discussion of the ends to be gained through such studies, with approval of the committee's suggestions given by the Council. A motion was made and seconded to appoint a committee to study the over-all question of medical and surgical fees, both private and industrial, but on vote the motion was lost.

5. *Report of the Council:*

(a) It was regularly moved, seconded and voted to add to the Report of the Council to the House of Delegates a section calling for support of the Student American Medical Association and urging the county societies to lend their support in this direction. The motion included the provision for subscriptions to the official Journal to be offered to Student A.M.A. members at a net cost to them of $1 per year, the remaining $2 per year required by postal regulations to be supplied out of general funds to be credited to the Journal.

(b) It was regularly moved, seconded and voted to add a section to the Report of the Council, calling for establishment within the Council of a Committee on Finance, through which all proposed appropriations in excess of the annual budget must pass and be approved before the Council acted on such proposals; this section would be offered only in the

event the proposed Constitution and By-Laws, which contain alternate provisions to give comparable protection, were not adopted.

6. *Committee on Committees:*

It was regularly moved, seconded and voted that the chairman appoint a committee to make recommendations for appointments to the Standing Committees. The chairman appointed John W. Green chairman and Ivan C. Heron, Jay C. Crane and C. V. Thompson as members.

7. *House of Delegates:*

(a) Dr. Lewis A. Alesen, Speaker of the House of Delegates, recommended that the hour of 3 p.m. on Tuesday, May 15, be designated as the meeting hour for the Administrative Members of California Physicians' Service, and it was regularly moved, seconded and voted that the order of business of the House of Delegates be set accordingly.

(b) It was regularly moved, seconded and voted that the chairman be authorized to invite Dr. John W. Cline, President-Elect of the American Medical Association, to address the House of Delegates and request the permission of the House of Delegates for this appearance.

8. *Committee on Medical Economics:*

(a) Dr. H. Gordon MacLean, chairman of the Committee on Medical Economics, reported on a study made by that committee of points of friction between physicians and underwriters of voluntary health insurance programs. The report showed that, aside from some minor complaints, practically all items in this category revolved around allegations of overcharges by physicians. The report made a comparison of indemnity allowances and actual charges by surgeons in a long list of actual cases and pointed out that while there was a variation in indemnities and fees in about 50 per cent of the cases studied, the variations were mainly of a nominal nature and that in not more than about 5 per cent of the total cases was there any indication of actual overcharging. The report made several recommendations for eliminating or reducing this type of complaint.

(b) Dr. MacLean reported on the projection of the report rendered by Ernst Dichter, Ph.D., in a study made for the Committee on Medical Economics on the question of individual physician-patient relationships. He recommended that members of the Council study this report thoroughly and that copies of it be sent later to all members of the Association.

9. *Emergency Maternal and Infant Care:*

Dr. Ray reported on a meeting held May 1, 1951, with the State Department of Public Health and representatives of the Children's Bureau on the question of reestablishment of the Emergency Maternal and Infant Care program of World War II. Two bills are now pending before Congress, one which would reestablish the former program and one which would grant a cash allowance for maternity care to the wives of enlisted men in specified grades. Dr. Ray discussed the possibility of suggesting that this program be handled through C.P.S. and similar Blue Shield plans.

On motion duly made and seconded, it was voted to support the American Medical Association in its opposition to one of the bills now before Congress (see also Item 7, 380th meeting).

10. *Public Policy and Legislation:*

Dr. Dwight H. Murray, legislative chairman, and Mr. Ben H. Read, executive secretary of the Public Health League of California, discussed numerous bills now pending before the State Legislature. To date a total of 5,246 bills has been introduced in the Legislature, about 10 per cent of which directly affect the practice of medicine or the public health. Many of the more important bills were discussed.

Discussion was held on the proposal to license practical or vocational nurses and, if so licensed, under which board would such licensing take place. Possible boards would be the Board of Medical Examiners, the Board of Nurse Examiners and the State Department of Public Health. It was agreed to discuss the matter further with the State Director of Public Health.

11. *Hospital Staff Appointment:*

Dr. Neil Dau brought before the Council the situation obtaining in his Councilor District, where a physician has not been appointed to a hospital staff and seeks aid from the Council in investigating the reason for such non-appointment. It was regularly moved, seconded and voted that this constituted a local matter in which the Council of the Association could not intervene.

12. *National Council of Churches of Christ:*

Dr. Dau discussed the appeal of the Council of Churches of Christ of America for a donation of $5,000 toward the cost of a mobile medical unit to serve migratory farm workers in the San Joaquin Valley. It was agreed to table this request temporarily, subject to its consideration at a later meeting during the 1951 Annual Session.

13. *Meeting Place for 1952:*

It was regularly moved, seconded and voted to hold the 1952 Annual Session at the Hotel Biltmore, Los Angeles.

Adjournment:

There being no further business to come before the meeting, it was adjourned at 4:00 p.m.

* * *

380th Meeting

The meeting was called to order by Chairman Shipman in Conference Room 6 of the Biltmore Hotel, Los Angeles, at 7:30 a.m., Sunday, May 13, 1951.

Roll Call:

Present were President Cass, President-Elect MacLean, Speaker Alesen, Vice-Speaker Charnock, Councilors Shipman, Lum, Ball, Crane, Henderson,

Dau, Ray, Montgomery, Pollock, Green, West, Heron, Thompson and Bailey, Secretary Daniels and Editor Wilbur. Absent for cause: Councilor Frees.

Present by invitation were Executive Secretary Hunton, Legal Counsel Hassard, Field Secretary Clancy, Legislative Chairman Dr. Dwight H. Murray, county society executive secretaries Waterson of Alameda-Contra Costa and Gillette of Fresno, Public Relations Counsel Clem Whitaker, Jr., Ned Burman and James Dorais.

Present by invitation during parts of the meeting were Dr. Lyell C. Kinney, chairman of the C.M.A. Cancer Commission and Mr. William T. Bender.

1. *Student American Medical Association:*

Mr. William T. Bender, a senior medical student at University of California, addressed the Council on the formation of school units of the Student American Medical Association. He reported on a meeting of the Student A.M.A. held in Chicago in December, at which 48 medical schools were represented by selected students. In February a meeting of the student council of the organization was held with three representatives of the A.M.A. He reported that 40 medical schools have now formed local units; in California, one unit has been formed at University of California, one is under formation at College of Medical Evangelists, the University of Southern California hopes to have a unit formed by next December, and Stanford has taken no steps to date toward such formation.

Mr. Bender outlined some of the aims of the Student A.M.A., requested that CALIFORNIA MEDICINE be made available to members of the student body at an annual rate of $1 per year, and that the Association throw its support behind the movement. After considerable discussion and a series of questions and answers, it was agreed to request Mr. Bender to address the House of Delegates in order to bring this information before the entire body.

2. *Cancer Commission:*

Dr. Lyell C. Kinney, chairman of the Cancer Commission, appeared to outline the program of the commission for the coming year. The program includes the employment of a medical director, one-half of whose salary is paid by the American Cancer Society, the distribution of a pamphlet to all general practitioners, one-half of which expense will be borne by A.C.S., a series of cancer conferences and other items which would total a cost of $19,000 for the Cancer Commission. It was regularly moved, seconded and voted that this sum be approved for inclusion in the budget for 1951-1952.

3. *Introduction of Dr. Charles Gordon Heyd:*

At this point, President Cass presented to the Council Dr. Charles Gordon Heyd of New York, the President's guest speaker, a former president of the American Medical Association and currently president of United Medical Service of New York, the Blue Shield Plan in the metropolitan New York area. Dr. Heyd expressed his pleasure in attending the Annual Session.

4. *Committee on Use of Radio:*

Dr. Dwight L. Wilbur, chairman of a committee to investigate the possible use of radio as a public relations medium, reported that the committee had considered the possibilities of two types of radio programs, one based on entertainment as a means of attracting an audience and one based on the use of a medical commentator. The latter type of program would entail the use of a professional radio performer as a commentator and would cost an estimated $125,000 annually. Mr. Clem Whitaker, Jr., supplemented Dr. Wilbur's report, which was given without recommendation, and outlined the costs involved in a commentator type of program, including a professional commentator at about $900 per broadcast, a research writer at about $750 monthly, the use of statewide radio networks at $668 to $856 per week and other costs bringing the total to an estimated $120,000 to $130,000 per year. On motion duly made and seconded, it was voted to table this proposal.

5. *Student American Medical Association:*

On motion duly made and seconded, it was voted to reiterate the approval made in the previous meeting, to make available to members of the Student A.M.A. subscriptions to the official journal at a rate of $1 per year, the budget to be adjusted to show $2 per subscription to be credited to the journal out of general funds, and this recommendation to include the discontinuance of the present publication, *Future M.D.*

6. *Governor's Conference on the Aging:*

Dr. Albert C. Daniels reported on his attendance at the Governor's Conference on the Aging, showing how the problems discussed at this meeting might well be translated into legislative proposals on a state or federal basis.

7. *Public Policy and Legislation:*

Dr. Dwight H. Murray, legislative chairman, asked the Council to go on record in opposition to a bill now before Congress to provide federal aid to medical schools and another bill, S. 1245, which would establish an Emergency Maternal and Infant Care program. On motion duly made and seconded, it was voted that an addendum to the Report of the Council be prepared to express support of the care of hardship cases in maternity care for wives of enlisted military personnel, on a basis which would not interfere with the practice of medicine or hospitalization and which would favor the use of existing voluntary organizations.

Adjournment:

There being no further business to come before the meeting, it was adjourned at 9:20 a.m.

381st Meeting

The meeting was called to order by Chairman Shipman in Conference Room 6 of the Biltmore Hotel, Los Angeles, at 7:30 a.m., Monday, May 14, 1951.

Roll Call:

Present were President Cass, President-Elect MacLean, Speaker Alesen, Vice-Speaker Charnock, Councilors Shipman, Lum, Ball, Crane, Henderson, Dau, Ray, Montgomery, Pollock, Green, West, Heron, Thompson and Bailey, Secretary Daniels and Editor Wilbur. Absent for cause: Councilor Frees.

Present by invitation were Executive Secretary Hunton, Legal Counsel Hassard, county society executive secretaries Gillette of Fresno and Young of San Diego, Wilton L. Halverson, State Director of Public Health, Public Relations Counsel Clem Whitaker, Jr., and Ned Burman.

Present by invitation during parts of the meeting were Drs. E. Vincent Askey, L. Henry Garland, R. Stanley Kneeshaw and William L. Bender.

1. *State Department of Public Health:*

Dr. Wilton L. Halverson, State Director of Public Health, paid tribute to the value of the Conference of Local Health Officers, which was legally established several years ago and which he stated had performed an invaluable service in public health work in California. He complimented Mr. Hassard on his active part in creating this conference.

Dr. Halverson reported on hospital construction funds under the jurisdiction of his department and stated that the Hospital Advisory Council to his department has adopted a policy of making grants for hospital construction on the basis of minimal rather than maximal needs, in order to limit these funds to fundamentals which will meet the needs of the community.

On the subject of licensing of emergency or industrial hospitals, Dr. Halverson requested the cooperation of the Council in studying the need for inspecting and licensing clinics, with a view toward possible repeal of that section of the law. It was pointed out that these clinics now come within the jurisdiction of the State Board of Medical Examiners and that the code sections administered by the Department of Public Health may no longer be needed.

2. *San Joaquin Valley Migrant Workers:*

Dr. E. Vincent Askey discussed the possibility of cooperating with the National Council of Churches of Christ of America, a subject discussed at an earlier meeting of the Council. Dr. Dau recommended that such cooperation be extended and it was regularly moved, seconded and voted to give help and encouragement to this council, with the thought of making a contribution upon the presentation of a feasible plan for carrying out the objectives of the Council for assistance to the migratory farm workers of the San Joaquin Valley. It was agreed that a committee should study this problem and the chairman appointed Drs. E. Vincent Askey, Neil Dau and Donald Cass to make such a study and report back to a later Council meeting.

Adjournment:

There being no further business to come before the meeting, it was adjourned at 9:00 a.m.

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382nd Meeting

The meeting was called to order by Chairman Shipman in Conference Room 6 of the Biltmore Hotel, Los Angeles, at 7:30 a.m., Tuesday, May 15, 1951.

Roll Call:

Present were President Cass, President-Elect MacLean, Speaker Alesen, Councilors Shipman, Lum, Crane, Henderson, Dau, Montgomery, Pollock, Green, West, Heron, Thompson and Bailey, Secretary Daniels and Editor Wilbur. Absent for cause: Vice-Speaker Charnock and Councilors Ball and Frees.

Present by invitation were Executive Secretary Hunton, Legal Counsel Hassard, county society executive secretaries Waterson of Alameda-Contra Costa, Gillette of Fresno, Young of San Diego, Public Relations Counsel Clem Whitaker, Jr., and Ned Burman.

Present by invitation during parts of the meeting were Drs. Earl Moody, Sam J. McClendon, Clifford Loos, Edwin L. Bruck, and Burt Davis.

1. *Medical Students:*

Dr. Burt Davis of Palo Alto urged the Council to take proper steps to encourage medical students to recognize the value of medical organizations. He suggested as one step the encouragement of university professors to maintain membership in medical societies, pointing out that some professors had dropped their memberships under current levels of state and county society dues.

2. *San Francisco Medical Society:*

On motion duly made and seconded, it was voted to recommend to the House of Delegates the issuance of a new charter in the name of San Francisco Medical Society (formerly San Francisco County Medical Society) upon the surrender of the charter previously issued.

3. *Invitation to American Medical Association:*

On motion duly made and seconded, it was voted to issue an invitation to the American Medical Association to hold its 1954 Annual Session in San Francisco.

4. *National Society for Medical Research:*

On motion duly made and seconded, it was voted to acknowledge receipt of the request of the National Society for Medical Research for a contribution of funds.

5. *Woman's Auxiliary to the C.M.A.:*

On motion duly made and seconded, it was voted to increase from $3,000 to $4,000 the annual appropriation of public relations funds made available to the Woman's Auxiliary for publication of its journal.

6. *National Conference on School Health:*

On motion duly made and seconded, it was voted to refrain from sending a representative to the National Conference on School Health. It was agreed that a representative to a former conference should be asked as to the value of such conferences to the Association.

7. *A.M.A. Council on Medical Service:*

On motion duly made and seconded, it was voted to request the C.M.A. delegates to the A.M.A. to ask that the Council on Medical Service of the A.M.A. be placed directly under the supervision of the A.M.A. Board of Trustees.

8. *Committee on Medical Economics:*

Dr. H. Gordon MacLean, chairman of the Committee on Medical Economics, recommended that the report entitled "Projection of the Dichter Report" be sent to all members of the Association and that copies of the complete original Dichter Report be made available to interested organizations. On motion duly made and seconded, these recommendations were adopted.

9. *1952 Annual Session:*

Dr. Albert C. Daniels, Secretary-Treasurer and Chairman of the Committee on Scientific Work, recommended that at the 1952 Annual Session the House of Delegates meet at 9 a.m. and the opening general scientific session start at 3 p.m. On motion duly made and seconded, these recommendations were adopted.

10. *Merced County Hospital:*

Drs. George B. Pimentel, James L. Dennis and Edward A. Jackson of Merced County placed before the Council a problem existing in that county in regard to the administration and policies of the county hospital. The Council was invited to send a committee to Merced to review the situation and was assured that the Board of Supervisors of the county would welcome such a committee. On motion duly made and seconded it was voted to instruct the Executive Committee to review the Merced County Hospital situation and to make recommendations.

11. *Committee on Clinical Material for Teaching Hospitals:*

Dr. William L. Bender, chairman of a special Committee on Clinical Material for Teaching Hospitals, presented the final draft of the committee's report on the acceptance of insurance cases for hospitalization by medical schools. The report included figures on four California and six out-of-state medical schools. On motion duly made and seconded, the report was accepted.

Adjournment:

There being no further business to come before the meeting, it was adjourned at 10:30 a.m.

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383rd Meeting

The meeting was called to order by Chairman Shipman in Conference Room 6 of the Biltmore Hotel, Los Angeles, at 7:30 a.m., Wednesday, May 16, 1951.

Roll Call:

Present were President MacLean, President-Elect Alesen, Speaker Charnock, Vice-Speaker Henry A. Randel, Councilors Shipman, Lum, Ball, Dau, Ray, Montgomery, Pollock, Green, West, Heron, Thompson, Bailey, H. Clifford Loos, Arthur E. Varden, J. Philip Sampson, and A. A. Morrison, Secretary Daniels and Editor Wilbur. Absent for cause: Councilor Frees.

Present by invitation were Executive Secretary Hunton, Legal Counsel Hassard, Legislative Chairman Dr. Dwight H. Murray, county society executive secretaries Waterson of Alameda-Contra Costa, Wood of San Mateo, Donovan of Santa Clara and Gillette of Fresno, Public Relations Counsel Clem Whitaker, Jr., and Ned Burman, past presidents Donald Cass and R. Stanley Kneeshaw.

1. *Election of Council Officers:*

On nomination duly made and seconded, Dr. Sidney J. Shipman was unanimously elected Chairman of the Council.

On nomination duly made and seconded, Dr. Donald D. Lum was unanimously elected Vice-Chairman of the Council.

On motion duly made and seconded, Dr. Albert C. Daniels was appointed Secretary-Treasurer of the California Medical Association.

On motion duly made and seconded, Dr. Dwight L. Wilbur was appointed Editor of the official Journal.

On motion duly made and seconded, the firm of Peart, Baraty & Hassard was appointed legal counsel to the California Medical Association.

2. *Appointment of Auditing Committee:*

The Chairman, with the consent of the Council, appointed Doctors Lum (chairman), Heron and Montgomery as members of the Auditing Committee for the 1951-1952 Association year.

3. *Invitations to Council Meetings:*

On motion duly made and seconded, it was voted to invite the Vice-Speaker of the House of Delegates to attend all Council meetings.

4. *Public Policy and Legislation:*

Mr. Hassard reported that a bill to define diagnosis had passed the State Senate. Another bill re-

lating to the revocation of licenses upon conviction of a criminal offense has likewise been passed by the Senate.

Discussion was held on a bill to provide federal, state and county aid to the permanently and totally disabled. On motion duly made and seconded, it was voted to draw up an appropriate resolution in opposition to this measure and to express this opposition to the American Medical Association.

5. *Establishment of Per Diem and Mileage Allowances:*

On motion duly made and seconded, it was voted to establish the per diem expense allowance of officers and councilors at $25 and automobile mileage allowance at 8 cents per mile, effective as of May 15, 1951.

6. *Compensation of Editor:*

Discussion was held on the compensation to be paid the Editor, the opinion being expressed that his present compensation was inadequate. The Executive Committee was asked to review this and report its recommendations to the next Council meeting.

7. *Advisory Planning Committee:*

Mr. Hunton, chairman of the Advisory Planning Committee, discussed the report of that committee on a "grass roots" public relations program for the Association, based upon strengthening the individual physician-patient relationship. The entire report of the committee was read to the Council, including recommendations for employment of three field representatives, establishment within the county medical societies of active programs in the public interest, publication of pamphlets which physicians might give to their patients and advertising of the availability of such pamphlets. A cost of about $80,000 was estimated. In executive session the Council voted approval of this program and its establishment under the direction of the Executive Committee.

8. *Committee on C.P.S. Functions:*

Discussion was held on the possible membership of a committee to look into various aspects of California Physicians' Service, as requested in a resolution approved by C.P.S. Administrative Members. On motion duly made and seconded, it was voted to authorize the Executive Committee to consider nominations for this committee and to make appropriate appointments.

9. *Time and Place of Next Council Meeting:*

It was announced by the Chairman that the next meeting of the Council would be held in San Francisco on Saturday, June 23, 1951. (Subsequently, the Chairman reset the date of the meeting to June 24, 1951, to avoid a conflict with other sessions.)

Adjournment:

There being no further business to come before the meeting, it was adjourned at 11:40 a.m.

SIDNEY J. SHIPMAN, M.D., *Chairman*
ALBERT C. DANIELS, M.D., *Secretary*

Executive Committee Minutes

Tentative Draft: Minutes of the 226th Meeting of the Executive Committee of the California Medical Association, Los Angeles, May 16, 1951.

The meeting was called to order by Dr. Donald D. Lum at 11:45 a.m., Wednesday, May 16, 1951, in Conference Room No. 6 of the Biltmore Hotel, Los Angeles.

Roll Call:

Present were President MacLean, President-Elect Alesen, Speaker Charnock, Council Chairman Shipman, Auditing Committee Chairman Lum and Secretary-Treasurer Daniels. Present by invitation were Executive Secretary Hunton and Legal Counsel Hassard.

Election of Chairman:

On nomination duly made and seconded, Dr. Donald D. Lum was unanimously elected Chairman of the Executive Committee.

Adjournment:

There being no further business to come before the meeting, it was adjourned at 11:50 a.m.

DONALD D. LUM, M.D., *Chairman.*
ALBERT C. DANIELS, M.D., *Secretary.*

In Memoriam

BEAUDOUX, HENRY A. Died in Saratoga, May 20, 1951, aged 70, following a long illness. Graduate of the University of Minnesota Medical School, Minneapolis, 1895. Licensed in California in 1924. Dr. Beaudoux was a retired member of the Santa Clara County Medical Association, and the California Medical Association.

✤

CLARK, DONALD K. Died in Oakland, April 18, 1951, aged 61, of cirrhosis of the liver. Graduate of the University of Louisville School of Medicine, 1911. Licensed in California in 1916. Doctor Clark was a member of the Alameda-Contra Costa Medical Association, the California Medical Association, and the American Medical Association.

✤

DOCK, GEORGE. Died in Altadena, May 30, 1951, aged 91. Graduate of the University of Pennsylvania School of Medicine, Philadelphia, 1884. Licensed in California in 1922. Doctor Dock was a retired member of the Los Angeles County Medical Association, a life member of the California Medical Association, and an Associate Fellow of the American Medical Association.

✤

MARCHAND, MALVIN C. Died in Wendover, Nevada, May 19, 1951, aged 37, in an automobile accident. Graduate of the University of Kansas School of Medicine, Lawrence-Kansas City, 1943. Licensed in California in 1948. Doctor Marchand was a member of the Butte-Glenn Medical Society, the California Medical Association, and the American Medical Association.

MORRISON, RICHARD J. Died in Pacific Palisades, May 29, 1951, aged 71, of heart disease. Graduate of Stritch School of Medicine of Loyola University, Chicago, 1918. Licensed in California in 1920. Doctor Morrison was a retired member of the Los Angeles County Medical Association, and the California Medical Association.

✤

MULLEN, ROBERT M. Died in San Marino, April 28, 1951, aged 43, of coronary artery disease. Graduate of Duke University School of Medicine, Durham, N. C., 1934. Licensed in California in 1937. Doctor Mullen was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

NEEDLES, JOHN W. Died in Redondo Beach, May 20, 1951, aged 40, of coronary artery disease. Graduate of the University of Southern California School of Medicine, Los Angeles, 1937. Licensed in California in 1937. Doctor Needles was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

✤

ROTH, HARRY A. Died in Long Beach, May 12, 1951, aged 44, of coronary thrombosis. Graduate of McGill University Faculty of Medicine, Montreal, 1930. Licensed in California in 1931. Doctor Roth was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

STURDEVANT, MATTHEW C. Died in Los Angeles, May 18, 1951, aged 43, of a brain abscess. Graduate of the University of Southern California School of Medicine, Los Angeles, 1936. Licensed in California in 1936. Doctor Sturdevant was a member of the Los Angeles County Medical Assocjation, the California Medical Association, and a Fellow of the American Medical Association.

VIAU, BENJAMIN. Died in Sacramento, May 19, 1951, aged 61, of coronary artery disease. Graduate of Stanford University School of Medicine, Stanford University-San Francisco, 1916. Licensed in California in 1917. Doctor Viau was a member of the Fresno County Medical Society, the California Medical Association, and the American Medical Association.

✤

WELFER, CLARENCE R. Died in Los Angeles, May 6, 1951, aged 56, of acute coronary occlusion. Graduate of the University of Pittsburgh School of Medicine, Pennsylvania, 1919. Licensed in California in 1922. Doctor Welfer was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

WILEY, EDWIN H. Died in Los Angeles, May 28, 1951, aged 73. Graduate of Northwestern University Medical School, Chicago, 1901. Licensed in California in 1905. Doctor Wiley was a member of the Los Angeles County Medical Association, a life member of the California Medical Association, and a Fellow of the American Medical Association.

✤

WILSON, HOMER S. Died in Lancaster, May 1, 1951, aged 68. Graduate of the University of Michigan Homeopathic Medical School, Ann Arbor, 1908. Licensed in California in 1921. Doctor Wilson was a retired member of the Los Angeles County Medical Association, and the California Medical Association.

✤

WOLD, ALVIN P. Died in Oakland, May 16, 1951, aged 55, of a brain tumor. Graduate of the University of Minnesota Medical School, Minneapolis, 1924. Licensed in California in 1928. Doctor Wold was a member of the Alameda-Contra Costa Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

Statement on Cancer Cures by the Cancer Commission of the C.M.A.

In recent months there has been a recrudescence in the daily press of claims for certain alleged cancer cures. Most of these receive the scant attention which they deserve and are soon forgotten. A few receive sensational publicity and are a source of considerable distress, both psychic and economic, to patients with cancer. In order to bring up to date the opinion of the Cancer Commission on this general question, it was resolved at the regular meeting of the Commission held in Los Angeles, May 1951, that a suitable statement bearing on this subject be prepared and issued to the press or to interested persons. The following is the statement as approved by the Commission:

From time to time there appear in the press, both public and professional, statements or claims regarding new cancer cures. Few of these statements or claims stand the test of time. Many prove a source of great mental and economic injury to persons suffering from cancer, to their relatives and friends.

The members of the Cancer Commission of the California Medical Association desire to give every aid in publicizing *reliable* methods of preventing and curing cancer. Many of them are actively engaged in research on the prevention, diagnosis and treatment of cancer. For that reason, the Commission believes it important to place some facts on record regarding this problem.

1. Cancer is an abnormal growth of tissue. The term "cancer" embraces an ill-defined heterogeneous group of diseases which vary greatly in natural history. Some types of cancer are very slow-growing and only locally invasive or malignant. Others are extremely rapidly growing and have already spread beyond likelihood of cure at the time an initial diagnosis is possible.

2. Owing to the variable nature of cancers or malignant tumors, it sometimes happens that there is difficulty in reaching a definite diagnosis even with the microscope. Sometimes conditions which strongly resemble cancer ultimately prove not to be, and go on to spontaneous cure. At other times, conditions which by all known tests are benign growths, turn out to be cancers. These situations are unusual, but indicate the need for adequate numbers of treated cases before claiming a cure.

3. The most reliable methods of cure for cancer are surgical and radiological treatment. A few special types of cancer can be temporarily controlled or relieved by chemical or drug treatment. In order to establish the reliability of a method of treatment, it is necessary for several patients to have been subjected to the method or drug in question, and to be studied for a period of years in order to confirm the fact that cure is permanent. It is therefore impossible to make dogmatic statements about the validity of many claimed cancer cures until a sufficient number of years has elapsed in order to permit proper assessment of results.

4. Most scientific workers do not make a secret of methods or drugs useful or potentially useful for human welfare. Most impartial and unbiased investigators make their method available for tests by some of the numerous agencies in this country created for assisting with such tests. The National Research Council has a Committee on Cancer Diagnosis and Treatment. Many universities have hospitals, clinics or individual investigators ready and willing to make scientific clinical studies on volunteer patients and other biological subjects. Only by prompt recourse to such tests will *facts* regarding apparent cancer cures become available to the public.

5. Not a single one of the several dozen cancer serums widely publicized in the public press during the last fifty years has stood the test of time.

Questions and Answers about C. P. S.

Question: **What is the status of the proposed new C.P.S. Fee Schedule which was distributed to physician members a few months ago?**

Answer: This proposed new fee schedule had been drawn up by the C.M.A. Fee Schedule Committee after lengthy study, and in March copies were sent to all C.P.S. physician members for their information. At the annual meeting of the C.P.S. House of Delegates in May it was voted to refer the proposed schedule back to the committee for further study, which is to be completed in six months. At the expiration of that time, the schedule will be resubmitted to the Council of C.M.A.

In conjunction with its action in directing further study, the House of Delegates also voted that, meanwhile, the existing C.P.S. fee schedule should continue to be used as the basis of payments for services rendered to C.P.S. beneficiaries. Therefore, while physician members have been provided with copies of the proposed schedule, they should not regard it as the "yardstick" of their payments for C.P.S. work—but should continue to refer to the existing fee schedule, the one dated September 1, 1949.

The answer to this question would not be complete without pointing out that, following the action taken by the House of Delegates, the C.P.S. Board of Trustees raised the percentage of payment under the existing fee schedule from 80 to 90 per cent, effective on all services performed on or after June 1. This is an "across the board" increase, applying to all procedures.

Question: **If a married man is enrolled in one C.P.S. group and his wife is enrolled in another C.P.S. group, how is the new income ceiling applied? Is it $4,200 or $3,600?**

Answer: Briefly, the answer is $4,200, but a fuller explanation is advisable so the reason will be clearly understood.

For services rendered on or after June 1, 1951, the $4,200 ceiling applies to *families of two or more persons* whose gross income for the preceding calendar year is less than $4,200. (Gross income is income from all sources, before taxes, and includes the husband and wife and dependent children under 19 years of age.) The $3,600 ceiling applies to single persons whose gross income is less than $3,600 for the preceding calendar year.

In the case of the husband and wife who are enrolled in separate C.P.S. groups, the reason the $4,200 ceiling applies is that they constitute a *family of two or more persons.* In other words, their C.P.S. income status is determined by their *family status,* not by the fact that they are enrolled separately (or singly) as C.P.S. beneficiaries.

Where there is doubt in the physician's mind as to whether the $4,200 or $3,600 ceiling applies to a patient, the best guide is to learn the patient's *family status.* If the family comprises two or more persons (including husband, wife and dependent children under 19 years—but not other relatives) the family income ceiling of $4,200 applies.

Question: **I have heard that there has been some difficulty in securing authorizations for the treatment of Spanish-American War veterans. Is this so?**

Answer: There is no difficulty, but physicians are reminded of a few differences in the handling of these accounts compared with other veteran cases:

1. All eligible Spanish-American War veterans must hold an honorable discharge; therefore no treatment should be given until an actual authority has been received, proving that eligibility has been established.

2. A Form 52 should be submitted in each case, and this form should list each and every disability for which the veteran seeks treatment. Such general diagnoses as "senile decay," "old age" or "general weakness" should be avoided.

3. A new request should be submitted for each change in diagnosis as treatment proceeds. These Spanish-American War veterans are entitled to care for any or all disabilities, but authority for each new condition must be secured.

4. The Veterans Administration will not grant retroactive authorization for treatment of a Spanish-American War veteran under any conditions, including emergency treatment. In cases of emergency, physicians should phone collect to the nearest VA regional office to get immediate authorization.

5. Visiting nurse service is available if necessary, but a special request form must be submitted. C.P.S. will forward these forms upon request.

6. Prosthetic appliances of all kinds are available for Spanish-American War veterans, but must be secured through the Prosthetic Appliance Division of the Veterans Administration, either in San Francisco or Los Angeles. Eye glasses are considered to be prosthetic appliances.

Question: **If the form 53-C for requesting continued treatment of a veteran is misplaced, may I make my request by letter?**

Answer: If this form is not at hand, request should be made on the physician's own letterhead to assure uninterrupted authorization. The request form for continued treatment is for the convenience of the physician's office in simplifying requests and as an aid to the C.P.S.-VA program in identifying the patient.

NEWS and NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

Dr. Lowell C. Goin, Los Angeles, was awarded a gold medal by the American College of Radiology during the recent American Medical Association session for distinguished and extraordinary service to the college and to the profession of radiology.

* * *

Dr. Emil Bogen, clinical associate professor of medicine at the University of California at Los Angeles School of Medicine, last month was elected president of the California Tuberculosis and Health Association for the year 1951-52. Dr. Bogen also was awarded the California medal for distinguished service in tuberculosis control.

* * *

The staff of Saint John's Hospital, Santa Monica, will hold its third annual **postgraduate assembly,** September 10 to 12, 1951, at the Elks Club, 21st Street and Wilshire Boulevard, Santa Monica. Dr. John C. Eagan, chief of staff, will be director of the assembly. Registration is open to all members of the medical profession.

SAN FRANCISCO

Dr. Edwin I. Bartlett, associate clinical professor of surgery and pathology at the University of California School of Medicine, San Francisco; **Dr. LeRoy H. Briggs,** William Watt Kerr Professor of Clinical Medicine, and **Dr. Howard C. Naffziger,** professor of neurological surgery and chairman of the department of neurological surgery, who are retiring as members of the faculty, were honored at the annual banquet of the school's alumni association, held last month.

* * *

The 79th annual meeting of the **American Public Health Association** will be held in San Francisco, October 29 to November 2. More than 5,000 specialists in public health are expected to attend this meeting and simultaneous meetings of the Western Branch of the A.P.H.S. and 38 related organizations. Dr. William P. Shepard will preside as president at the meeting. Headquarters for the main meeting will be the San Francisco Civic Auditorium.

Among the related organizations meeting with the association are: American Association of Registration Executives, American Association of Schools of Public Health, Association of Maternal and Child Health and Crippled Children's Directors, Association of State and Territorial Health Officers, Commissioned Officers Association of the U. S. Public Health Service, Conference of Municipal Public Health Engineers, Conference of Professors of Preventive Medicine, Conference of Public Health Veterinarians, Conference of State and Provincial Public Health Laboratory Directors, Conference of State Directors of Public Health Education, Society of Public Health Educators, Conference of State Hospital Personnel, Conference of State Sanitary Engineers, Council of State Directors of Public Health Nursing, Civil Affairs Committee of Military Government Public Health Society, Public Health Cancer Association, and National Organization for Public Health Nursing.

At the 1951 meeting of the American Psychiatric Association, Dr. Jurgen Ruesch, associate professor of psychiatry at the University of California School of Medicine, and his associates at the Langley Porter Clinic, Robert E. Harris, Ph.D., Carole Christiansen, M.A., Martin B. Loeb, B.A., Sally Dewees, M.S., and Annemarie Jacobson, M.D., were presented the **Hofheimer Award for research in psychiatry.** The prize was awarded for a sociopsychological study of patients with duodenal ulcer. The results of the inquiry were published in book form by the University of California Press in 1948.

GENERAL

Dr. Frank H. Krusen of Rochester, Minnesota, chairman of the **Baruch Committee on Physical Medicine and Rehabilitation,** announced recently that the committee had achieved its goals and was discontinuing its activities. At the same time Mr. Bernard M. Baruch, New York City, the sponsor of the committee, which has been active since November 1943, announced that he was watching the institutions to which he had made grants, on recommendation of the committee, and that it was his object to make further grants "to those who undertake the work with enthusiasm and beneficial results." The committee had been formed by Mr. Baruch to develop and advance the special field of medicine devoted to the diagnosis and treatment of disease by physical agents and to the rehabilitation of disabled persons.

* * *

Expressing concern over the **waste of medical personnel** and facilities entailed in uncoordinated programs being carried out by various government agencies at a time when military and civilian defense demands are of grave importance, 21 members of the National Advisory Board of the Doctors Committee for Improved Federal Medical Services have petitioned Congress for immediate legislative action based on recommendations of the Hoover Commission on federal medical services.

* * *

The third annual postgraduate course on **Psychiatry for the General Practitioner** will be offered at the University of Colorado Medical Center July 26, 27, 28, 1951. The course will deal with prevalent psychiatric concomitants in general practice, with emphasis on psychotherapy. The practical nonspecialized aspects of psychiatry in general medicine will be emphasized. Information regarding registration and fees may be obtained from the Office of the Director of Graduate and Postgraduate Medical Education, 4200 East Ninth Avenue, Denver 7, Colorado.

* * *

Delegates to the annual spring convention of the American Council of Christian Churches unanimously passed a resolution reaffirming the organization's **stand against socialized medicine.** "Freedom of the individual, freedom of the doctor, and freedom of medical research are essential to the preservation of a free society," the resolution stated.

POSTGRADUATE EDUCATION NOTICES

UNIVERSITY OF CALIFORNIA SCHOOL OF MEDICINE—Medical Extension, San Francisco

Gynecological and Obstetrical Conference:

August 29 through 31, 1951. Room 104, University Extension Building, 540 Powell Street, San Francisco. Fee: $50.00.

Ophthalmology:

September 10 through 14. Medical Center, Parnassus and Third avenues.

This course, for specialists, is a continuation of programs offered in 1947, 1948, and 1949.

Evening Symposia in Medicine:

Sept. 10 through Nov. 26 (every Monday evening). Medical Center, Parnassus and 3rd avenues.

This is a series of evening exercises for general practitioners in the form of symposia on topics of particular interest to them.

Contact: Stacy R. Mettier, M.D., Medical Extension, University of California Medical Center, San Francisco 22, California.

STANFORD UNIVERSITY SCHOOL OF MEDICINE

Postgraduate Medical Courses for Practicing Physicians:

In cooperation with the San Francisco Department of Public Health and the San Francisco Hospital.

September 10, 11, 12, 13, 14, 1951.

Morning Courses: Monday, Tuesday, Wednesday, Thursday and Friday—8:30 a.m. to 12 noon.

COURSE 1—GENERAL MEDICINE (San Francisco Hospital—Limited to 20 physicians). Discussion of development, diagnosis, treatment and prognosis of various diseases will stem from cases presenting problems in internal medicine.

COURSE 2—GENERAL SURGERY (Stanford Hospital—Limited to 20 physicians). Selected general surgical topics will be reviewed in a series of ward rounds, clinics and lectures. Emphasis will be on the practical aspects of surgical treatment.

COURSE 3—UROLOGY FOR THE GENERAL PRACTITIONER (Stanford Hospital—Limited to 20 physicians). A practical course in the diagnosis and treatment of common urologic conditions. Detailed consideration will be given to office treatment, the use of modern antibiotics, infertility in the male, pyelographic interpretation, and to indications for and types of cystoscopic and operative procedures.

COURSE 4—PRACTICAL DERMATOLOGY (Stanford Hospital—Limited to 25 physicians). A practical course designed to emphasize diagnosis and treatment of the common dermatoses. Instruction will consist of numerous case presentations and discussions.

COURSE 5—DIAGNOSIS AND TREATMENT OF TUMORS (Stanford Hospital—Limited to 25 physicians). Cancer of the most frequent and accessible sites will be emphasized. Differential diagnosis, standard treatment and recent therapeutic developments will be stressed. The presentations will be didactic with critical discussion in which students will be invited to participate actively.

COURSE 6—GENERAL SURGERY (San Francisco Hospital—Limited to 30 physicians). General surgical ward rounds; groups of ten to single instructor.

COURSE 7—SURGICAL ANATOMY (Stanford Hospital—Limited to 20 physicians). Dissection of special regions and instruction and practice in the technique of various operations will be conducted in the dissecting room.

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Afternoon Courses: Monday, Tuesday, Wednesday, Thursday and Friday—1:30 p.m. to 5:00 p.m.

COURSE 8—GENERAL MEDICINE (Stanford Hospital—Limited to 15 physicians). Clinical problems as they are affected by advances in fundamental knowledge will be discussed in selected fields. The subjects presented will be: pulmonary physiology and disease, hemorrhagic states, diabetes mellitus, syphilis, nutrition and the vitamins, electrolyte and water metabolism and the clinical use of cortisone and ACTH.

COURSE 9—SURGICAL ANATOMY (Stanford Hospital—Limited to 20 physicians). Dissection of special regions and instruction and practice in the technique of various operations will be conducted in the dissecting room.

COURSE 10—CARDIOLOGY (San Francisco Hospital—Limited to 25 physicians). Recent advances in clinical cardiology with sections devoted to electrocardiography and newer diagnostic methods and to present day medical and surgical treatment of cardiac disease.

COURSE 11—OBSTETRICS AND GYNECOLOGY (Stanford Hospital—Limited to 25 physicians). Informal discussions and demonstrations concerning amenorrhea, dysmenorrhea, disturbed uterine bleeding, birth trauma lesions, bleeding in pregnancy, therapeutic abortion, breech presentation, use of forceps, endometrial cancer and cytology in relation to incipient malignancy.

COURSE 12—PSYCHIATRY FOR GENERAL PRACTITIONERS (Stanford Hospital—Limited to 25 physicians). A presentation of the principles of psychiatry in general medical practice. Emphasis is on the practical procedures in diagnosis and treatment of commonly encountered disorders, especially in the psychosomatic area. Case presentation and panel discussion.

COURSE 13—ENDOCRINOLOGY (Stanford Hospital—Limited to 25 physicians). The course will summarize the physiology, the diagnosis and the treatment of disorders of the pituitary gland, the adrenals, the thyroid, and the male and female gonads. The management of diabetes, the metabolic effects of ACTH and cortisone, the parathyroids and bone disease, and the clinical uses of the sex steroids will be discussed. Lectures, case demonstrations and panel discussions.

COURSE 14—PEDIATRICS (Stanford Hospital—Limited to 25 physicians). Therapy in Pediatrics: Recent advances in therapy as it applies to infants and children will be discussed.

INFORMATION

You and Blue Shield

[The author of the following article is Frederick W. Slobe, M.D., Assistant Director and Medical Director, Blue Cross Plan for Hospital Care and Illinois Medical Service, with headquarters in Chicago, and Medical Director, Illinois Medical Service. The article is reprinted, by permission, from the *Illinois Medical Journal* issue of March 1951.]

You, as a physician, are a part of Blue Shield . . . so, naturally, you are concerned about it. You are a part of it because Blue Shield is always sponsored by a medical society. In Illinois, at least 51 per cent of the doctors in a county must sign cards as participating physicians, and the county medical society must take official action approving a Blue Shield Plan before it can become operative in that county. So the physicians really underwrite Blue Shield in a moral sense at least; occasionally in a financial sense too—for example, should a Plan get into financial difficulty, physicians might be expected to accept a reduced schedule of allowances; also, in service Plans with a low income limit the doctors may subsidize the Plan partially. The State Department of Insurance considers this backing of Blue Shield by a majority of physicians in a county to be most significant and necessary. Once the cards have been signed, most Blue Shield Plans, if of the indemnity type, make no distinction between a participating physician and one who has not signed the cards . . . making payments to all according to the schedule of allowances, the only requirement being that the physician to whom payment is made must be licensed to practice medicine and surgery in all its branches in the state where services are rendered. So you are really a part of Blue Shield whether or not you signed a card because of action taken by your medical society.

You know Blue Shield is an important part of the voluntary insurance movement. It has 16 million members and is growing rapidly. It operates on the not-for-profit principle in order that the maximum percentage of each premium dollar be utilized to pay or help pay for physicians' services. Blue Shield believes in the profit motive in business, in free enterprise, competition and incentive. But the type of protection offered by many private insurance companies in the past did not seem to be a good enough "buy" to the consuming public. And the popularity of Blue Cross was an important factor in influencing medical societies to establish Blue Shield as a companion Plan. Besides, there is room for all in the battle against compulsory health insurance. It is an obvious fact that the competition by Blue Cross and Blue Shield has been a decided influence in effecting improvements by the private insurance companies as regards contractual benefits. These improvements, in turn, act as a constant stimulus to the non-profit Plans. The result is a steadily expanding service to the public.

You may have wondered why there are several Blue Shield Plans in Illinois. That is simply because county societies in various sections have seen fit to organize their own Plan . . . usually in cooperation with a Blue Cross Plan. Those who fear "bigness" and alleged monopoly think this is sound. Others, however, are fearful about this and point to the success in our sister state, Michigan, where the Blue Shield Plan, "Michigan Medical Service," sponsored by the state medical society, has a membership of over 1,900,000 members. They are also concerned about future confusion in overlapping areas within a state, friction, diminished efficiency and impaired public relations as a result.

Of importance to you is the fact that Blue Shield is commonly known as "The Doctors' Own Plan." The responsibility and obligation implied here are obvious. If a Blue Shield Plan is badly administered . . . if it gets into financial difficulty . . . if its contractual provisions are inequitable . . . if the physicians do not cooperate . . . if the subscribers have legitimate complaints not satisfactorily answered, both the Blue Shield movement and the medical profession suffer. If the doctors' charges are exorbitant and out of proportion to the patient's ability to pay, the subscriber rightfully feels that membership in Blue Shield has been of no appreciable value because of the disproportion between the Blue Shield allowance and the doctor's fee. The same would apply if a physician, because of his patient's having Blue Shield coverage, increased his usual fee by an amount equal to the Blue Shield allowance. In such instances, the protective value of insurance coverage is lost.

Blue Shield does not fix the doctor's fee (if the Plan is of the indemnity type); and free choice of doctor and hospital are maintained always. Blue Shield does not practice medicine; and it is not within its scope to question either the doctor's charges, operative indications or procedures employed. The medical societies, however, *are* keenly interested; having either initiated or approved the program, they have a responsibility and an obligation too . . . and that is why county or state medical societies have professional relations or advisory committees for Blue Shield with the exclusive function of carefully observing the relationship between the physicians, Blue Shield and the public. These committees are concerned about public relations

and grievances. They contact physicians by letter or phone and may refer matters to appropriate committees for final disposition.

Since physicians have this responsibility, it follows that they should control Blue Shield Plans and such is the case. The majority of trustees are physicians although lay representation is recognized as an indicated procedure.

The public is the consumer of medical care and the consumer must be protected if the voluntary Plans are to serve their purpose as the chief bulwark against compulsory health insurance.

Blue Shield, then, is *your* contribution toward supplying a nonprofit medical care Plan to help pay or pay medical costs. It is *your* contribution to furnish an important component in the voluntary health insurance field . . . as opposed to the compulsory political type. So your support is essential. This includes explaining it to your patients, friends and business contacts. Your secretary needs to know about it too. Filling forms out promptly and completely is important. The more information you furnish, the better can the disbursing department of Blue Shield evaluate your cases. There is no violation of confidence involved since every Blue Shield member authorizes this upon joining. And unless your fee is stated, Blue Shield cannot obtain statistics as to what percentage of doctors' bills it pays.

In general, there are two types of Blue Shield Plans—the "indemnity" type and the "service" type.

THE INDEMNITY PLANS

In the "indemnity" Plans, payments are made to physicians, according to a fixed schedule of allowances, the physician being privileged to charge the patient the difference between his fee and the allowance received. Hence the allowance neither fixes nor bears any relationship to the physicians' charges. There are many, especially leaders of organized labor, who have voiced dissatisfaction with the indemnity principle. The chief objection has been that, where indemnity contracts prevail, too small a percentage of the physician's fee is covered by the Blue Shield allowance.

This objection might be obviated: (1) if payments under an indemnity schedule were large enough to equalize the average prevailing charges; and (2) if physicians, in such instances, would charge the average patient approximately what the Blue Shield allowance amounted to. This would require a moderate increase in subscription rates but appeals to the physician because it does not conflict with his traditional method of practice and billing.

THE SERVICE PLANS

In the "service" type, where the member or the member's family income does not exceed a stipulated amount, the physician agrees to accept the Blue Shield allowance as payment in full, but is privileged to charge an additional amount to equalize his fee when the family income exceeds the stipulated level. Thus, most service contracts are really a combination of both types — being of a "service" type when family income does not exceed a certain level . . . and an "indemnity" type when income does exceed such level.

The "service" Plans appeal to the public because no additional payment need be made to the physician unless the family income exceeds a stipulated amount, in which case the Plan operates on the indemnity principle. Some Plans have more than one service contract with different income limits; for example, $3,000 and $5,000. Selling at different rates, they fit the financial resources of the members; also, the allowances in the latter may range from 30 to 100 per cent higher than in the former. The decision as to income level is usually left to the physicians—sometimes the member is asked to fill out a brief form; rarely is difficulty experienced on this score. If this income level is set at $5,000 for example, it would include about 80 per cent of the population in most communities . . . and physicians' fees for this 80 per cent would be fixed at the Blue Shield allowance. This upsets the traditional system and is disquieting to many physicians. There are others who feel that this is part of the physicians' contribution to the battle against socialized medicine. They feel that some change and adjustment is necessary to meet the demands of masses of people despite all our efforts toward education. Physicians are inherently altruistic; monetary gain has never been their motivation; they know that no financial reward can ever be measured to compensate them for having saved a life; they do not expect their services to be compensated on the basis of a lawyer or broker; and many of them are perfectly willing to subsidize a Blue Shield Plan. Financial loss, however, does not appear to accrue where well integrated service Plans are in operation with a high enough income limit and a correspondingly adequate schedule of payments. In such instances, the income of physicians appears to be maintained at the previous level. In this connection, Dr. Louis F. Middlebrook of Connecticut Medical Service has said: "It has been my impression from talking with both participating physicians and with subscribing member-patients that because of rapid settlement of claims and 100 per cent collections, payments on cases that otherwise would have been staff cases without remuneration for the physician, and on others which would have been impossible or difficult to collect, the net result has been increased remuneration for the physician and improved services to the patient." One reason for this is a sufficiently high rate to enable payments substantially higher than exists in most indemnity Plans.

The public is invariably enthusiastic about service Plans. People say it is the profession's positive and satisfactory answer to political medicine. The trend is strongly toward the service Plan philosophy and it behooves us to study the matter impartially. We should probably ask ourselves why it should not be successful here if it is successful in other states.

Indeed, the "service" philosophy . . . namely, fur-

nishing complete or virtually complete hospital or medical service instead of dollars . . . is the unique and most popular feature of most Blue Cross and Blue Shield Plans.

If the Blue Shield Plans in Illinois are successful, it will be largely because of your attitude, understanding and cooperation. Of those favoring compulsory health insurance, some think so because of unfavorable experiences with physicians' charges; others because they believe the average person cannot pay the cost of a hospitalizing illness. The first criticism can be met through education of the profession and in the exceptional, justified case by referral to the grievance committee of a medical society. The second criticism can be met by voluntary insurance if most, if not all, of the medical bill is paid and if coverage is available to most of the people. A third requisite is that the rate charged for such coverage is one which the people can afford to pay. It is difficult to reconcile these needs without having recourse to the "service" type of certificate and rendering available individual as well as group enrollment.

Dr. H. L. Childs has said that the "success of free enterprise system depends upon providing the best possible service to the largest number of people at prices they can afford to pay." This statement is applicable to medical service too. Blue Shield aims to help people do this. How far it will succeed depends on you.—F. W. S.

BOOK REVIEWS

PHYSICAL DIAGNOSIS. By Ralph H. Major, M.D., Professor of Medicine, The University of Kansas. 4th edition. Illustrated. W. B. Saunders Company, Philadelphia. 1951. 446 pages. $6.50.

The fact that this textbook on physical diagnosis has reached a fourth edition bespeaks its worth. It is one of the standard books on the subject. In each edition the author has improved the work by correction of inevitable errors, by improvements and additions to the text and by the further use of diagrams and illustrations. The fourth edition continues this trend.

The book is well organized. The material is presented in the sequence commonly followed in the performance of a physical examination. The text is well written and easy to read. An enlivening feature is the author's frequent quotation from classical descriptions together with interesting and pertinent anecdotes. Dr. Major believes, with Osler, that "when you can, read the original descriptions of the masters, who with crude methods of study, saw so clearly." Pertinent new facts and new interpretations are included. The material is thoroughly up to date. The whole is blended into a concise, interesting and easily readable text.

An outstanding feature of the book is the liberal use of diagrams and photographs. Many have been added and others have been improved since the earlier editions. They effectively supplement the text and greatly add to the interest of the book. Each chapter is concluded with a bibliography which documents the material of the text. As one might expect, the bibliography contains many references to classical descriptions which would be particularly valuable to those who are interested in the history of medicine or to those interested in further study.

All in all, this book is an excellent text on physical diagnosis. It presents the subject readably and effectively, with thoroughness and with perspective. It should be useful to the student, teacher and practitioner.

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PRINCIPLES OF PUBLIC HEALTH ADMINISTRATION. By John J. Hanlon, M.S., M.D., M.P.H., Associate Professor of Public Health Practice, School of Public Health, University of Michigan. The C. V. Mosby Company, St. Louis, 1950. $6.00.

This book should be interesting and valuable for every physician who recognizes professional responsibilities beyond those of private practice. From it, he can enhance his understanding of the motives and methods of public health workers. Hanlon devotes a section of 80 pages to the philosophy and background of public health, and maintains that successful workers in this field must be strongly idealistic. The shocking, abominable state of affairs under which life was lived a century and more ago is recounted, and the growth of a community conscience which led to the alleviation of these conditions is clearly set forth by the extensive use of quotations from the leaders in medicine, sanitary science, and social welfare of the nineteenth and early twentieth centuries. Reading this, one can see how present-day public health workers may be impatient at delay in bringing all of our present knowledge of preventive medicine to all the people.

The introductory section also includes an extensive development of data on the economic value of public health work. Examples drawn from this should be effective in convincing laymen that support of well-designed preventive medical programs is a good investment.

Physicians interested in medical economics and the interrelationships of government and medicine will find valuable background material on the growth of the Federal government programs which have modified activities in local health departments so markedly. Hanlon appears to be an open-minded conservative in his discussion of these matters. He devotes little space to the consideration of medical treatment or hospitalization as a public health measure, even for such diseases as tuberculosis and syphilis. He repeatedly emphasizes the important role to be played by private practitioners in a well-developed public health program. In his presentation of doctor-patient-government relationships, he strives to present facts on all sides of the issues and in general to let the reader draw his own conclusions.

The chapters on managing the work of others are done well. Although much of the material is obviously plain common sense, its presentation in a systematic and orderly way will help one to remember it and to use it in those times of stress when it is most needed. Although this material is addressed to a specific group, the principles and methods outlined can be used profitably in the private office, the home, or in the professional society equally well. Other topics covered include fiscal management, legal considerations, public relations, and the programs under the principal health department divisions, such as vital statistics, child and maternal health, and so on. Industrial hygiene services are slighted.

The main criticisms refer to form, rather than content: There is a frequent lack of juxtaposition between the tables and figures and the related text. The captions of the tables and figures are not as clear as they might be, in some instances.

On the whole, this is a well-balanced, well-written, informative book, certain to be of value to public health workers, and likely to be interesting to many others.

* * *

CANCER AS I SEE IT. By Henry W. Abelmann, M.D., The Philosophical Library, New York, 1951. 100 pages. $2.75.

This little book presents the author's interpretation of his observations and research on cancer in the last 45 years. The theme developed throughout is that all malignant disease is caused by a microscopic organism, and that all types of cancer are different manifestations of the invasion of this organism. Genetics and irritation are considered as predisposing factors in diminishing cell resistance, but the real cause is this pleomorphic parasite which he designates as a "mold fungus" and later as a "germ virus."

Included in this common etiology are all types of carcinoma, sarcoma, pernicious anemia, leukemia, Paget's disease, Hodgkin's disease, mycosis fungoides, and precancerous hyperplasia (which is called cancer granuloma). The type of cancer produced is due to the stage of pleomorphism and the reaction specific to each type of cell which it attacks. Melanomas are caused by a black mold fungus and chloroma by a green mold fungus.

The pleomorphic stages of this cancer parasite are considered to cover the spectrum of microscopic biology from a mold to the ultramicroscopic virus. In the mold stage, infiltration of the interstitial tissues causes a chronic inflammatory cancer granuloma. In the virus stage the parasite penetrates the cell membrane of a somatic cell and makes it a cancer cell, giving that cell all of its malignant characteristics.

The author considers the various inclusion bodies reported in cancer from the time of Virchow and San Felecis to Dr. Irene Miller, not as contaminants but as different forms of the organism that causes cancer. "The pleomorphic germ endowed with different properties can explain all the

diverse and curious phenomena met with in cancer." "Cancer is caused by the infection of a body cell, and there are therefore as many kinds of cancer as there are different kinds of body cells."

The major source of infection by the cancer germ is considered to be from the soil and through foods. Thus, care in what we put into our stomachs is considered the first line of defense in the prevention of cancer.

In addition to developing his unique and unproved hypothesis, Dr. Abelmann emphasizes the need of early diagnosis, public education and periodic examination. He suggests that a national cancer day should be set aside to make the public cancer-conscious.

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DIMENSIONAL ANALYSIS FOR STUDENTS OF MEDICINE. By Harold A. Abramson, M.D., Assistant Clinical Professor of Physiology, Columbia University. The Josiah Macy, Jr., Foundation, 565 Park Avenue, New York 21. 1950. 41 pages. $1.00.

A sharp tool is a terrible temptation—for instance, mathematics. As a former sinner, the reviewer sympathizes with Dr. Abramson, but unhappily the author's dimensional analysis and sympodism and psychomotive forces are not impressive. His introductory statement, "No amount of purely mathematical reasoning can ever take into consideration the complexity of the emotional factors," may some day prove exaggerated, in consequence of vector analysis; but even granting the power of mathematics, this reviewer is not a bit converted to Dr. Abramson's eagerness to pump that kind of reasoning into psychiatrists.

Students of medicine, to all of whom Dr. Abramson directs his book, will (1) as a body prefer to work at the care of patients, or (2) if in research medicine, prefer fuller treatment of the subject, such as Griffin's "Mathematical Analysis" and Fisher's "Statistical Methods for Research Workers."

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METHODS IN MEDICINE—The Manual of the Medical Service of George Dock, M.D., Sc.D., Formerly Professor of Medicine, Washington University School of Medicine; Formerly Physician-in-Chief, Robert A. Barnes Hospital, St. Louis. A Comprehensive Outline for Clinical Investigation, Management and Treatment of Patients with Various Medical Disorders. By George R. Herrmann, M.D., Ph.D., Professor of Medicine, University of Texas Medical Branch at Galveston. Second edition, completely revised. 488 pages. The C. V. Mosby Company, St. Louis, 1950. $7.50.

This book is presented as a practical bedside guide for the clinical investigation of the common as well as some of the more rare medical conditions. It is intended for interns, residents, and practitioners, and details what the author considers minimal requirements for diagnostic study and medical management. Dr. Herrmann calls it a revision of the manual which he published 26 years ago, but actually it is a new book. Despite this the author, unfortunately, has hung on to certain items which, though useful in 1925, are of historical interest only in 1951.

The book has both good and bad points. It can be very handy as a compendium, listing a variety of information in its contents. It includes data on methods of history and physical examination, laboratory procedures and therapeutic methods. The material shown has very definite interest, but the reviewer finds himself not infrequently at a loss to explain why some items are in and others out. For instance, in a short summary of antibiotics, such a little-used one as Nisulfazole is given mention in the quite limited space available. The bibliography is also spotty: References are given for the management of renal stones and peripheral vascular disease, but none for irritable colon, nephritis or rheumatoid arthritis. Some of the methods are followed through thoroughly, but many others end up in a blind alley. In this regard one may mention the discussions on biopsy of muscle (page 163) and on the technique for counting peripheral blood (pages 44-48). If one did not already know the techniques, he would have to look further than this book.

The style is very authoritative, which may irritate some readers, particularly when statements are inaccurate; for example, on page 277 the author states that the Takata test "has been found to be positive in any disease in which the serum globulin is over 3 per cent" (an erroneous conclusion of the year 1934).

The book cannot be recommended to the practitioner to employ for casual reference or detailed investigation on a given case. On the other hand, in a hospital which may adopt it as a methodology, it has a field of usefulness as a vade mecum for the intern.

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SKULL FRACTURES AND BRAIN INJURIES. By Harry E. Mock, M.D., Consulting Surgeon, St. Luke's Hospital, Chicago, Associate Professor Emeritus of Surgery, Northwestern University Medical School. The Williams and Wilkins Company, Baltimore, 1950. 806 pages. $13.50.

A very comprehensive review of head injuries, skull fractures and brain injuries, written from the standpoint of the general surgeon. The author has had a most extensive experience in the management of head injuries and presents a very complete account of his wide experience. Since the vast majority of head injuries are seen by those other than neurosurgeons, this volume represents an excellent addition to the library of every practicing physician.

It is written in too great detail to be used as a textbook, but can be heartily recommended as a complete source of reference concerning the diagnosis, management and complications of head injuries. Dr. Mock presents a plan of management of these patients which, if adequately followed, no doubt would result in a definite lessening of mortality from such injuries. Many controversial points are discussed, and included therein are the views of numerous specialists in neurological surgery.

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THE CLINICAL USE OF RADIOACTIVE ISOTOPES. By Bertram V. A. Low-Beer, M.D., Associate Professor of Radiology, University of California Medical School, San Francisco, Calif. Charles C. Thomas, publisher, Springfield, Illinois, 1950. $9.50.

Part One, 128 pages, concerns physics, measurements, and radiation hygiene, with seven tables and 27 figures, a list of 43 books, and references to 40 authors, not keyed into text. Part Two, clinical applications, fills the rest of the book, including bibliography of 11 books and 327 references keyed into text. There is also an appendix of useful factual data and dosage computations and an extensive table of isotopes. The index is fairly detailed, occupying 25 columns, and omits authors. This part has 58 figures, also four pages of color plates concerning the author's investigation of P_{32} on blotting paper for treatment of skin lesions. Many of the figures are graphs, which with 34 tables give a good quantitative understanding.

This volume, in contrast to so many "edited" textbooks recently published, is all by one hand, which gives it a good unity of treatment. The coverage is very broad. The numerous clinical investigations with tracers and for therapy are grouped under the isotope concerned (12 elements). Therapy with P_{32}, Na_{24}, I_{131} and Co_{60} is covered in a chapter of 65 pages, preceded by 16 pages on the computation of internal dosage. The author is a practitioner of radiation therapy of long and wide experience, with a thorough grounding and containing professional contacts for nuclear physics and radiobiology. This wedding of theory and clinical experience in the one mind gives the book an unusually firm foundation. With the advances attained already and the bright future promise of radioisotopes in clinical medicine, every radiologist would do well to read this book and keep it handy.

It is a serious duty to be prepared to take proper part in isotope committees as they are being set up in more and more hospitals so as to take advantage of the availability of these valuable tools (isotopes) through the Atomic Energy Commission. The fact that the science and art is moving fast, and that the book will soon be outdated, does not lessen its present usefulness.

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CHECK—Community Health Educator's Compendium of Knowledge. By Clair E. Turner, A.M., Ed.M., D.Sc., Dr.P.H., Professor of Public Health Emeritus, Massachusetts Institute of Technology. The C. V. Mosby Company, Baltimore. 1951. 266 pages. $3.00.

If some bright and enterprising surgeon with an encyclopedic memory, photographic mind, and years of successful experience would pack into a small reference-size manual of 225 pages the essentials of the basic sciences as they apply to the surgical art, the psychological and physical characteristics of the patient, important diagnostic criteria and surgical indications, briefly outline the technique covering the major procedures, and at the same time append a wealth of social material, that author would do for surgery what Professor Clair E. Turner has done for the art of health education.

This neat little volume in a board binding with the catchy title, "Check," cannot be summarized, abridged, or abbreviated, because it is pure essence in itself. The author presents his ideas in three parts: Part One, Basic Principles; Part Two, Working with People; Part Three, Media of Group Communication. In addition, there are a useful appendix and a helpful bibliography.

While Professor Turner presents his material from the standpoint of one primarily interested in public health education, and while the activities described and the factual material contained are directed toward that end, he calls upon a basic knowledge of the human individual and the manner in which that individual reacts under different circumstances to propose a method of leading him into a favorable acceptance of new ideas concerning his own health and the environment that contributes to it in such a comprehensive manner that the techniques described would be equally applicable to any phase of human relations.

Part One, "Basic Principles," deals with the nature of community health education, the development of public health education and the scope of health education, and outlines where health education occurs. The functions, personal qualifications and techniques of the community health educator are indicated. As a part of this latter discussion, a job performance check list is presented consisting of a group of requirements that could well be imposed upon a worker in any field of endeavor. Just a few of these will illustrate the kind of thinking involved:

Carries assignments through to completion.

Carries out assignments promptly.

Organizes work well.

Makes accurate analysis of situations.

Discriminates between essentials and nonessentials.

Is capable of meeting emergencies.

Keeps up to date on improved techniques and procedures in work.

Accepts responsibility for errors of own making.

Chapter VI of Part One, entitled "Motivation," states that public health education is concerned primarily with the development of attitudes and actions and presents a series of reasons as determined by experience why individuals do and do not accept a program of hygienic practices. On page 37 of this same chapter, fundamental human wants are analyzed and the health educator is advised to build his program in such a way as to appeal to these basic human wants. "Health is an abstraction. To the sick it means freedom from the distressing symptoms of disease. To the well person and the general public its value is primarily what it enables one to be, to do, and to acquire." The four categories to which appeal is made are:

1. The want for a feeling of personal worth.
2. The sex want (the family and the race).
3. The want for a livelihood (fear of being poor).
4. The want for variety.

In Part Two is presented a wealth of material on the techniques of working with people. This is outlined step by step beginning with the individual conference, proceeding to group thinking, covering general meetings and community organizations and campaigns. The importance of the individual and his own personality in presenting appealing ideas to other individuals and to groups is emphasized. Suggestions are made as to the kind of approaches most likely to succeed and those doomed to failure.

Part Three, "Media of Group Communications," is more specific in its analysis of the available media of communicating ideas. The principles underlying group communications are elaborated. Skillful writing, effective speech, radio and television, newspapers, printed matter, magazines, books, letters and questionnaires, pictures and graphs, motion pictures and exhibits, all receive technical evaluation even to the point of instructions as to how to read and correct a galley proof or as to what constitutes the best type of halftone for reproduction.

The style and mode of this compendium are indeed different and original with the author. After reading and thoroughly enjoying Professor Turner's "Check," your reviewer was faced with just one question: Have we in medicine been too busy, too stupid, or just too lazy so that it has been necessary for a layman to take the lead in an activity which primarily should be our responsibility?

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TEXTBOOK OF PHYSIOLOGY AND BIOCHEMISTRY. By George H. Bell, B.Sc., M.D. (Glasg.), F.R.F.P.S.G., F.R.S.E., Professor of Physiology in the University of St. Andrews at University College, Dublin; J. Norman Davidson, M.D., D.Sc. (Edin.), F.R.F.P.S.G., F.R.I.C., F.R.S.E., Gardiner Professor of Physiological Chemistry in the University of Glasgow; and Harold Scarborough, M.B., Ph.D. (Edin.), F.R.C.P.E., Professor of Medicine in the Welsh National School of Medicine of the University of Wales. The Williams and Wilkins Company, Baltimore, 1950. 918 pages. $9.00.

Structural biochemistry without relation to function holds little interest for the medical student or practitioner, or for that matter, for the investigator of the dynamic aspects of medicine. Likewise, physiology without a basis in chemistry is inadequate. The three authors of this book, a physiologist, a biochemist and a clinician, unite their efforts in the production of a skillfully and interestingly written introduction to the subjects of mechanical and chemical physiology. Chapter I is a general introduction with the following opening statement:

"The subjects of Physiology and Biochemistry comprise the study of living matter at two different levels. The biochemist studies biological systems at the molecular and atomic level, while the physiologist is concerned with the intact organ, or the whole organism. Both have a dynamic outlook, and indeed biologists in general at the present time are more interested in the function of living matter than in its structure. Physiologists and biochemists are concerned essentially with changes in the organism as it reacts to changes in its environment."

Another statement in the introductory chapter deserves quoting:

"At one time the organic basis for a patient's symptoms could be established only at the post-mortem examination. The trend in modern medicine and surgery, however, is to study the living patient more and more intensely in order to understand not only his symptoms but the way in which normal physiological and biochemical processes have broken down, for disease is coming increasingly to be thought of as a disordered physiology in which the compensatory mechanisms have been overstrained."

Chapters II to VIII describe the essential present-day information concerning the basic chemical structure of the body: Carbohydrates, lipids, the proteins, nucleic acids and nucleoproteins, enzymes, water, and minerals. Chapters IX to XXI, XXV, and XXXII to XXXIV, inclusive are devoted to foods and vitamins, transport, digestion, absorption and metabolism of foods and respiration and biological oxidations and reductions. The remaining portions of the book are devoted to circulation, excretion, locomotion, sensation and reflex centers, functions of different parts of the central and autonomic nervous systems, the endocrine glands, reproduction, heredity, growth and senility. The text is profusely illustrated with tables, charts, drawings, photographs and photomicrographs. It is remarkable how much important information is to be found in this relatively small volume and how successfully the material has been organized and presented, not only for teaching those who approach the subject for the first time, but also for those who would use the book for reference. It is well indexed.

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PHARMACOLOGY. By Michael G. Mulinos, M.D., A.B., A.M., Ph.D., Associate Professor of Physiology and Pharmacology, New York Medical College. Oxford University Press, New York, 1951. 484 pages. $5.00.

This book is unique in the field of pharmacology in that it is written in outline form rather than as straight textual matter. This no doubt makes for ease in finding the particular information for which the busy practitioner is looking, but for the medical student approaching the subject for the first time it seems scarcely good pedagogy. The author also makes the same mistake so many other textbook writers make, especially those writing in the field of pharmacology; he has introduced the subject by giving a long list of definitions, dosage rules, principles of administration, general principles of pharmacology and classification of drugs before the student has learned any of the properties of drugs which would make it possible for him to comprehend the principles. Such an approach requires rote memory on the part of the student. For those who approve this style of teaching this is the best "small" book in the American market. There are however actually 466 pages of text outline and tabular material, and the book is therefore small only in comparison with such encyclopedic works as Sollmann's "Manual of Pharmacology" or Goodman and Gillman's "Pharmacological Basis of Therapeutics."

The reviewer has read this book with mixed admiration and disappointment. There are many more practical points concerning uses of drugs than are found in the larger treatises but it is difficult to find an analytical or critical evaluation of a drug. The book is purely descriptive. There are excellent tables for orientation and comparison of drugs, and if one is looking for a direct statement of site and manner of action, he can quickly find it, but one looks in vain for experimental or clinical evidence for the statements. There is a good selection of toxicological effects but little attention to site and manner of action of poisons.

The author gives more detail for the administration of drugs than is usually found in a textbook of pharmacology but important factors governing administration, such as fate and excretion of drugs, are given inadequate treatment. For example, there is no discussion of carinamide in relation to the excretion of penicillin, and Brodie's excellent work on the metabolism of acetanilid and similar drugs is overlooked.

Unfortunately, the book was completed before the appearance of the latest edition of the United States Pharmacopeia (U.S.P. XIV) so that new names and official status of many drugs are not included. There has been a failure to bring the bibliography up to date. There are many statements which are not acceptable to most pharmacologists and critical and experienced clinicians, such as that barium chloride is useful in treatment of the Stokes-Adams syndrome, that cyclopropane induces adequate muscular relaxation, and the incomplete statement that the active principles of digitalis "are glycosides, made up of an aglycone possessing the cardiac activity, and a carbohydrate portion called digitoxose." However, the author is to be commended for the statement that "there is no proof that the purified principles of digitalis are superior to the powdered leaf or its tincture, except in the rate of absorption or the route of administration."

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HEART DISEASE—ITS DIAGNOSIS AND TREATMENT. By Emanuel Goldberger, B.S., M.D., Associate Attending Physician, Montefiore Hospital, New York; Lecturer in Medicine, Columbia University. 90 Illustrations. Lea & Febiger, Philadelphia. 1951. 651 pages. $10.00.

This is a well written and excellently illustrated book on diseases of the heart and great vessels. The diagrams of roentgen-ray films of the heart in the various clinical states are especially well executed for teaching the patterns of chamber enlargements. As would be expected of this author, electrocardiography is briefly but well presented for each of the clinical states discussed. It is well indexed with an adequate but not massive bibliography including a careful choice of key articles recently published.

The remarkable characteristic of this work is the inclusion of a mass of information with unusual clarity and brevity. There is an avoidance of repetition by cross-references. Brevity has the advantage of making readily accessible the outstanding diagnostic and clinical features of each disease entity with its basic structural and functional abnormalities. However, such restriction of space limits description of the variations that are often observed in many of the clinical conditions covered, most notably rheumatic fever, rheumatic heart disease and myocardial infarction.

The organization of the book separates clinical syndromes from the disease entities, which is generally satisfactory, but results in discussions of angina pectoris and myocardial infarction without developing the concept of borderline states of coronary circulatory insufficiency.

There are excellent and well accepted plans of therapy, including anticoagulant drugs, ACTH, cortisone, quinidine and pronestyl, as applied by the author, which should furnish the practitioner many tools for treatment of cardiac patients. As would be expected, when an author draws liberally from personal experience, there will be conflict between his and other opinions as to the values and dangers of some of these procedures; for example, the uniform use of dicumarol or tromexan in treatment of myocardial infarction. These drugs may not be worth using on mild cases of myocardial infarction, especially where trained technicians are not available.

The book should serve as a valuable source of ready reference for all medical practitioners in the broad field of cardiology, excluding peripheral vascular diseases, and a guide to explore in greater detail those subjects which are only briefly included. Although the author emphasizes the practical aspects of cardiology, such as bedside diagnostic methods and the relation of surgery and pregnancy to the cardiac patient, he also presents briefly the most recent technical developments as exemplified by cardiac catheterization and electrokymography.